UCSB

CHEMICAL LiFE CYCLE COLLABORATIVE

CLICC WEBINAR 3

EXPOSURE & TOXICITY, PREDICTIVE LIFE CYCLE IMPACT ASSESSMENT, UNCERTAINTY, AND APPLICATION OF CLICC

DINGSHENG LI, RUNSHENG SONG,
YUWEI QIN, JESSICA PERKINS, STEFANO CUCURACHI

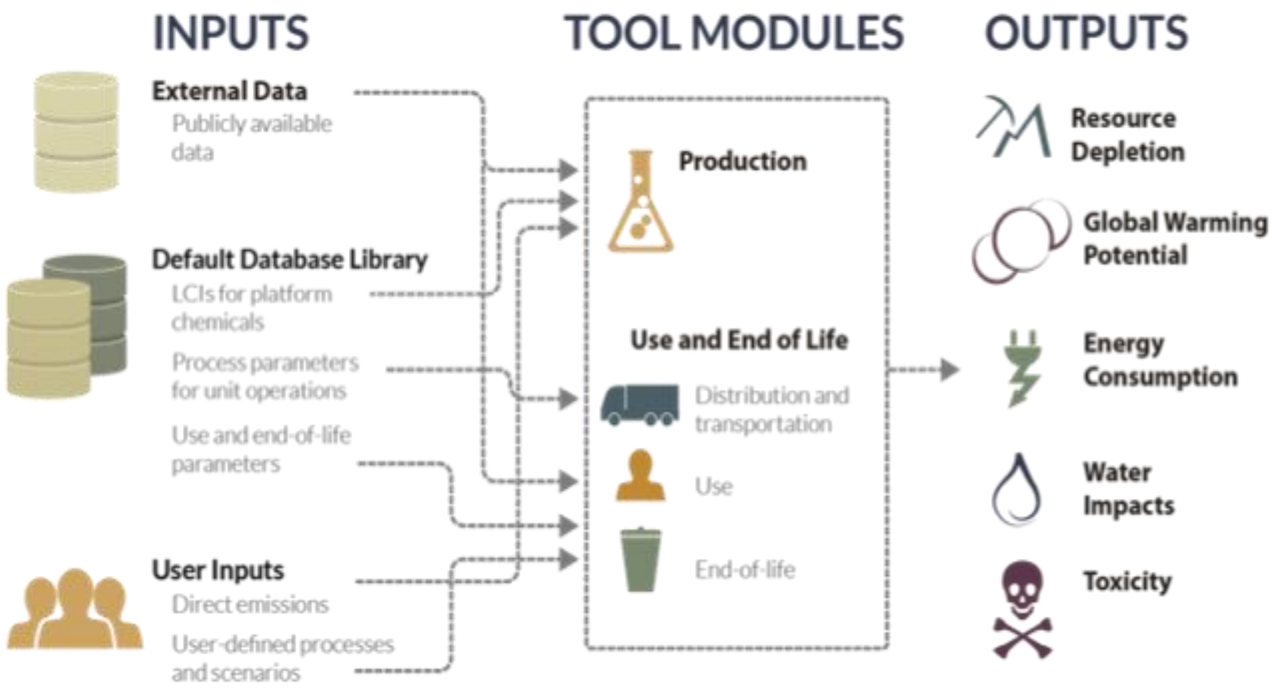
10/7/2016

CLiCC Webinar series

- Webinar 1
  - 9/14/2016
  - Life Cycle Inventory
- Webinar 2
  - 9/30/2016
  - QSAR, Release, Fate & Transport
- Webinar 3
  - 10/7/2016
  - Exposure & Toxicity, Predictive Life Cycle Impact Assessment, Uncertainty, application of CLiCC
- All webinars are recorded and available for viewing on clicc.ucsb.edu

CLiCC project

- U.S. EPA funded UCSB to develop a tool that can rapidly estimate the environmental impacts of a chemical life-cycle based on limited information



Exposure Module

- Why do we need exposure models

Environmental fate of chemicals

Human health impact assessment

Exposure Models

- Far-field exposure models
  - Traditionally employed in life cycle impact assessment (LCIA)
  - Inhalation, ingestion
- Near-field exposure models
  - Indoor exposure
  - Personal care products
  - Inhalation, dermal absorption
- Internal organ specific exposure model
  - Use of physiologically based toxicokinetic (PBTK) model
  - Concentration of chemicals in various organs after exposure

Exposure Models

- Input to exposure models
  - Concentration of chemicals in different media
  - Various parameters of physico-chemical properties
- Output from exposure models
  - Total amount intake ($kg/kg_{bodyweight}$)
  - Daily amount intake (kg/day, $kg/kg_{bodyweight}/day$)
  - Intake fraction ($kg_{intake}/kg_{emitted}$)
- Ready to assess health risk

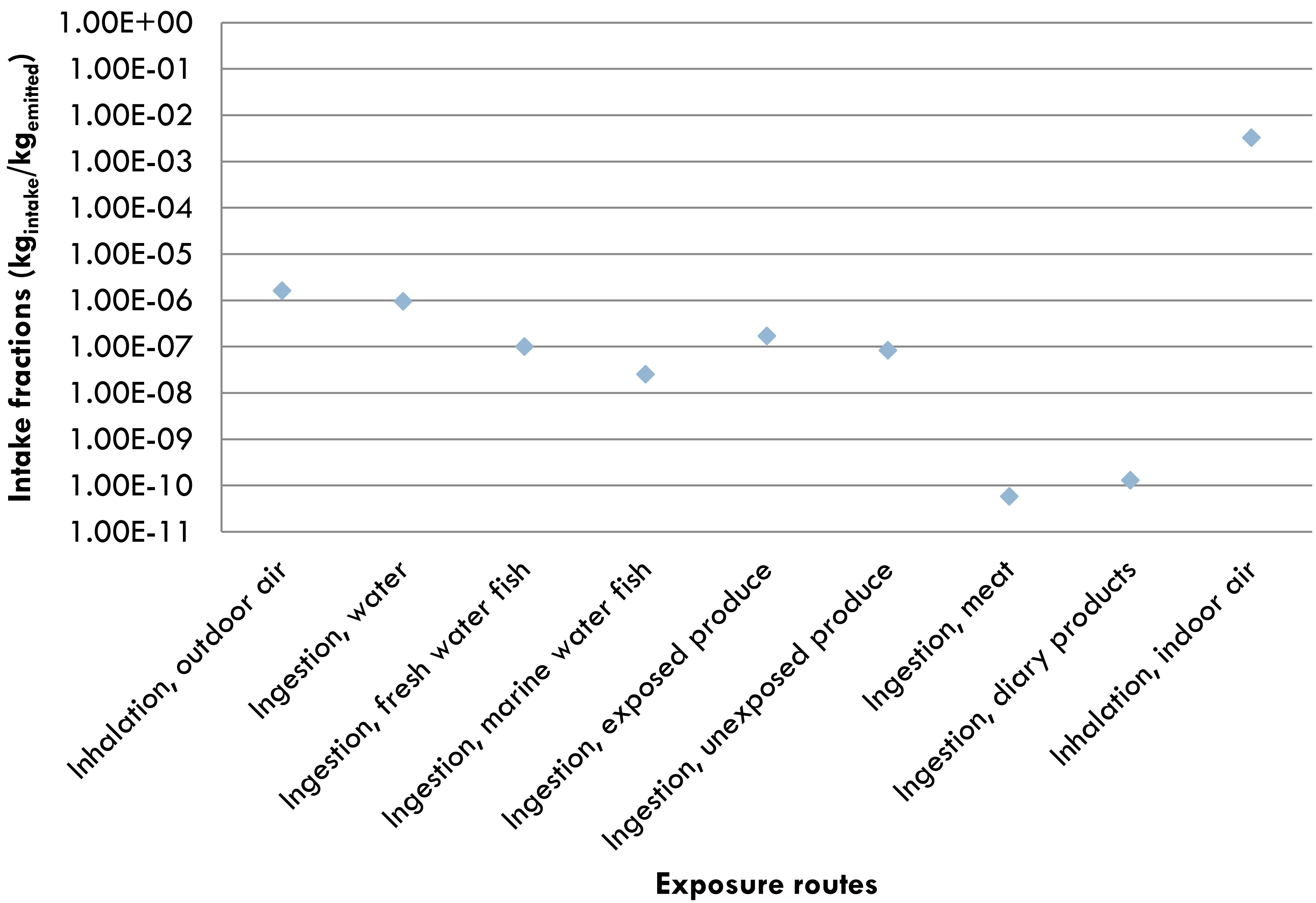
Exposure Models

- Far-field exposure models most suited for
  - Byproducts, pollutants, pesticides, etc.
  - No need to address indoor exposure/dermal exposure
  - Directly linked with CLiCC Fate & Transport module

Exposure Models

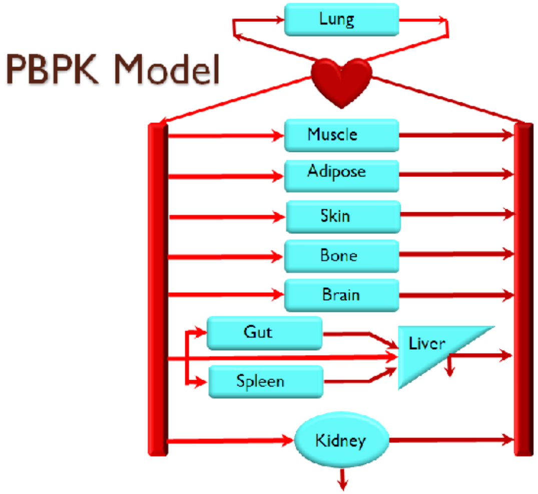
- Near-field exposure models most suited for
  - VOCs that are released from products used indoors
  - Occupational setting
  - Directly applied to skins such as shampoo, lipsticks, lotions, etc.
  - Linked with the CLiCC Release module

Exposure Models

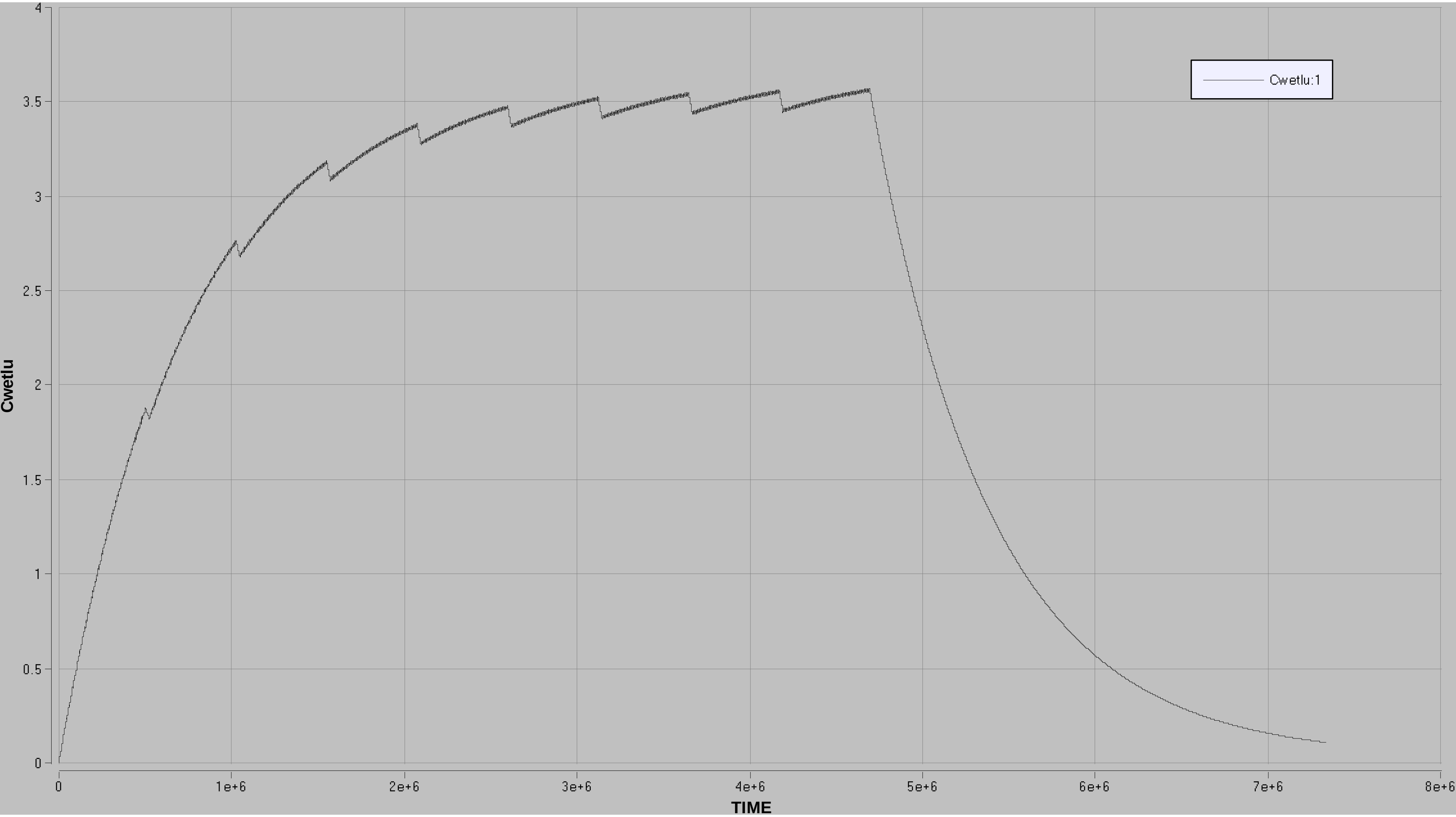


Exposure Models

- Internal organ specific models most suited for
  - Chemicals requires higher accuracy or dynamic of exposure
  - Chemicals with richer physiological kinetic data

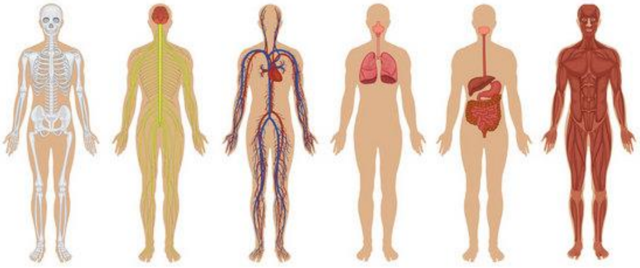


Exposure Models



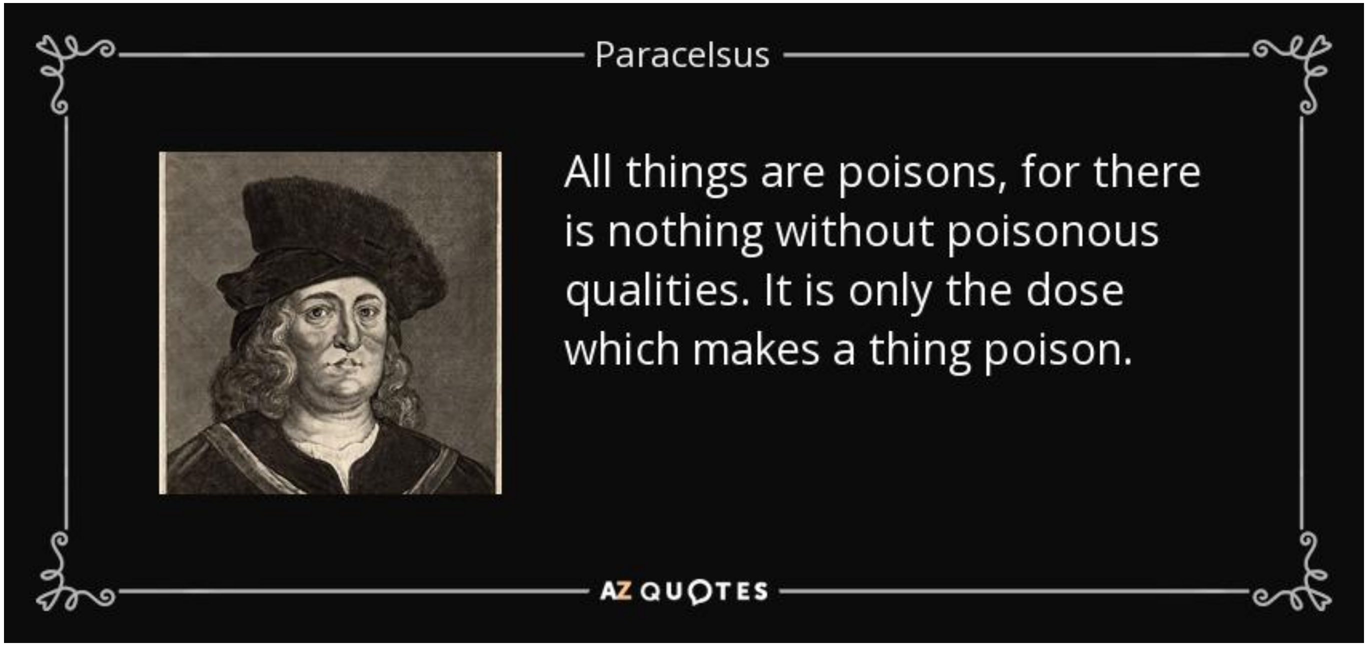
Toxicity

- Chemicals can harm us in many different ways
  - Carcinogenicity
  - Developmental toxicity
  - Mutagenicity
  - Genotoxicity
  - Reproductive toxicity
  - Irritation and sensitization



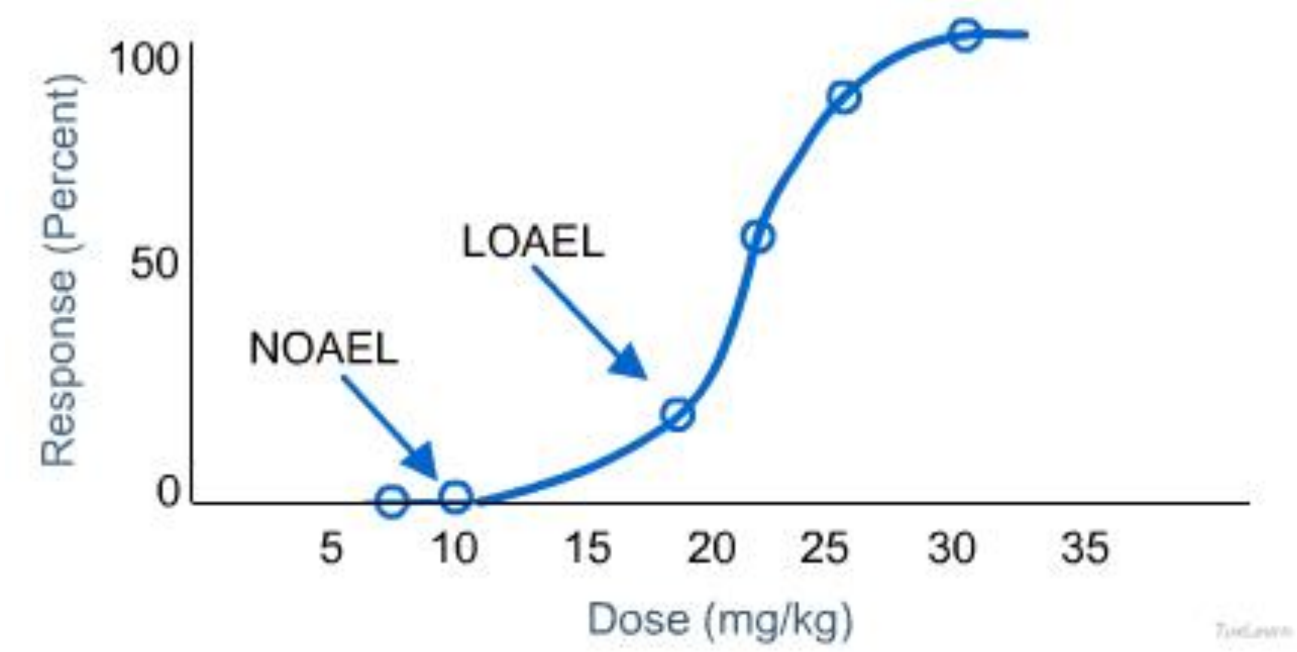
Toxicity

- Some QSAR models can predict various endpoints qualitatively (yes/no)
- How can we assess toxicity quantitatively?



Toxicity

- The dose-response relationship
  - NOAEL (no observed adverse effect level)
  - LOAEL (lowest observed adverse effect level)
  - ED_{50} (effective dose for 50% of population)



Toxicity

- Effect factor, a metric to quantitatively describe the toxicity of chemicals to human health. The unit for EF_{hum} is (cases/kg_{intake})
- Based on the assumption of linear dose-response relationship
- $EF_{hum} = 0.5/ED_{50}$
- Estimating ED_{50} is key

Toxicity

- Epidemiology studies (tier 1)
  - Most ideal, but rare
  - Direct use of the slope factor observed in these studies

Toxicity

- Chronic animal studies (tier 2)
  - For carcinogenic effects

$$ED_{50h,ingestion} = \frac{TD_{50a,t,ingestion} \cdot BW \cdot LT \cdot N}{AF_a \cdot AF_t \cdot 10^6}$$

$$ED_{50h,inh} = \frac{EC_{50a,t,inh} \cdot INH \cdot LT \cdot N}{AF_a \cdot AF_t \cdot 10^6}$$

  - TD_{50} and EC_{50} based on animal tests, in mg/kg-day or mg/m^3
  - BW, body weight (70 kg); LT, lifetime (70 years); N, days per year (365.25 days/year); Af_t (correction factor for exposure duration, 2 for subchronic, 5 for acute)

Toxicity

- AF_a, according to Vermeire et al., 2001

Type	CF interspecies (-)	Average bodyweight (kg)
human	1.0	70
pig	1.1	48
dog	1.5	15
monkey	1.9	5
cat	1.9	5
rabbit	2.4	2
mink	2.9	1
guinea pig	3.1	0.750
rat	4.1	0.250
hamster	4.9	0.125
gerbil	5.5	0.075
mouse	7.3	0.025

Toxicity

- Chronic animal studies (tier 2)
  - For non-carcinogenic effects

$$ED_{50h,ingestion} = \frac{NOEL \cdot 9 \cdot BW \cdot LT \cdot N}{AF_a \cdot AF_t \cdot 10^6}$$

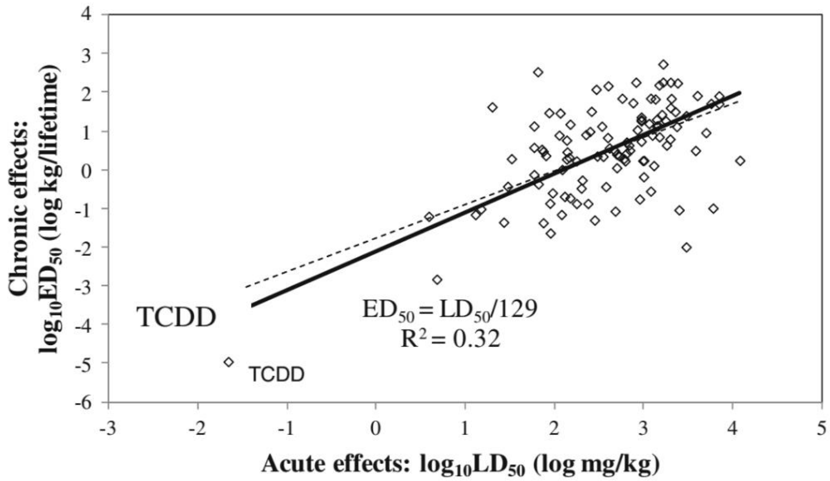
$$ED_{50h,ingestion} = \frac{LOEL \cdot 2.25 \cdot BW \cdot LT \cdot N}{AF_a \cdot AF_t \cdot 10^6}$$

$$ED_{50h,inh} = \frac{NOEC \cdot 9 \cdot INH \cdot LT \cdot N}{AF_a \cdot AF_t \cdot 10^6}$$

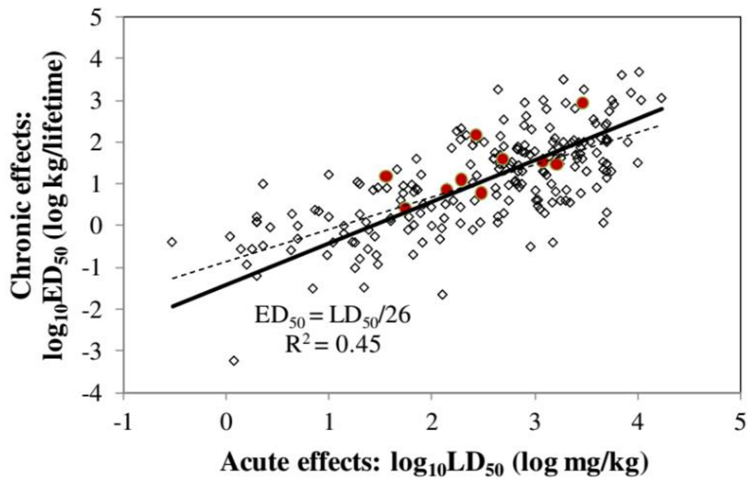
$$ED_{50h,inh} = \frac{LOEC \cdot 2.25 \cdot INH \cdot LT \cdot N}{AF_a \cdot AF_t \cdot 10^6}$$

Toxicity

- Acute animal studies (tier 3)
  - More data available with LD_{50} (dose lethal to 50% population)
  - Regression model to extrapolate from acute to chronic



Cancer effect

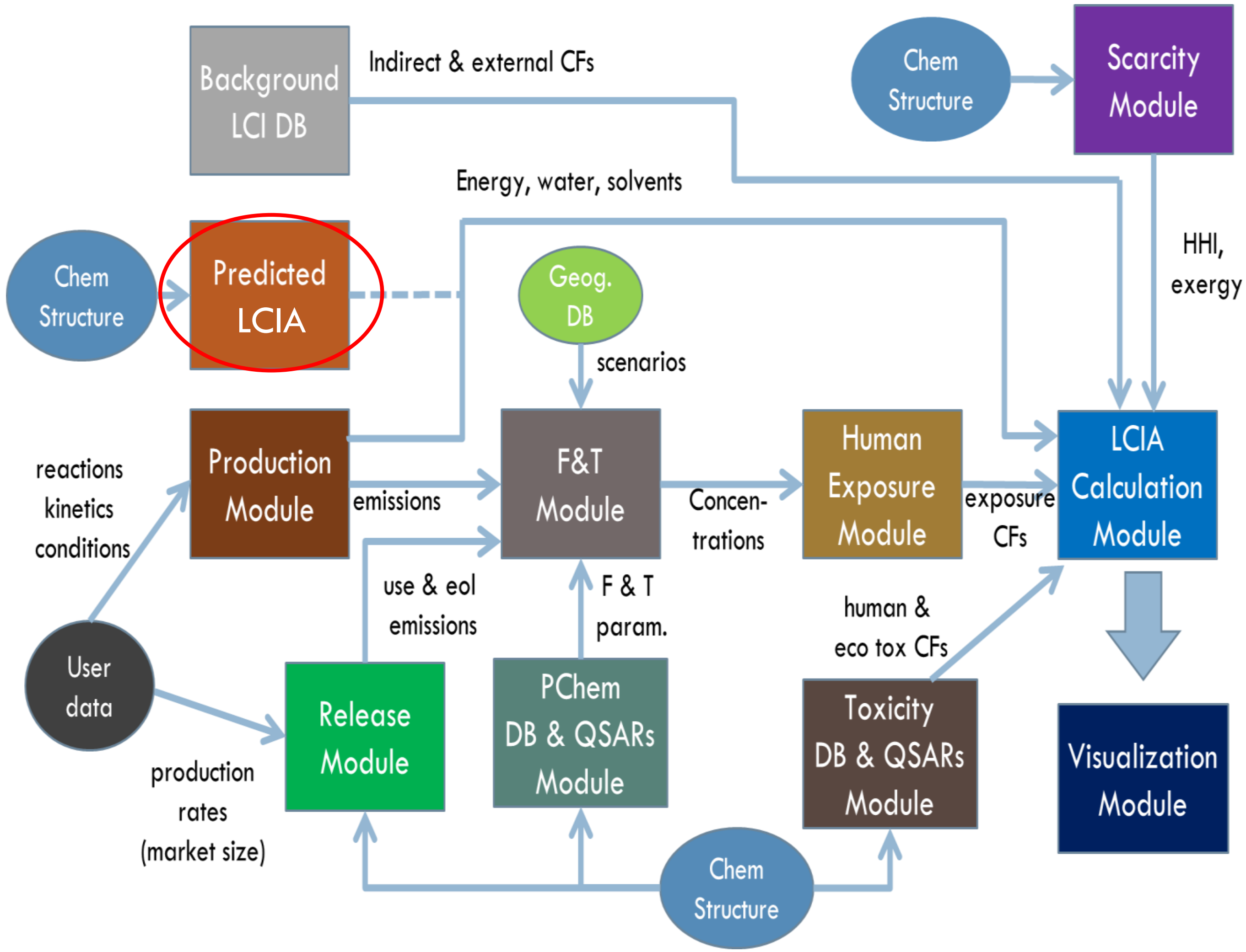


Non-cancer effect

Exposure & Toxicity

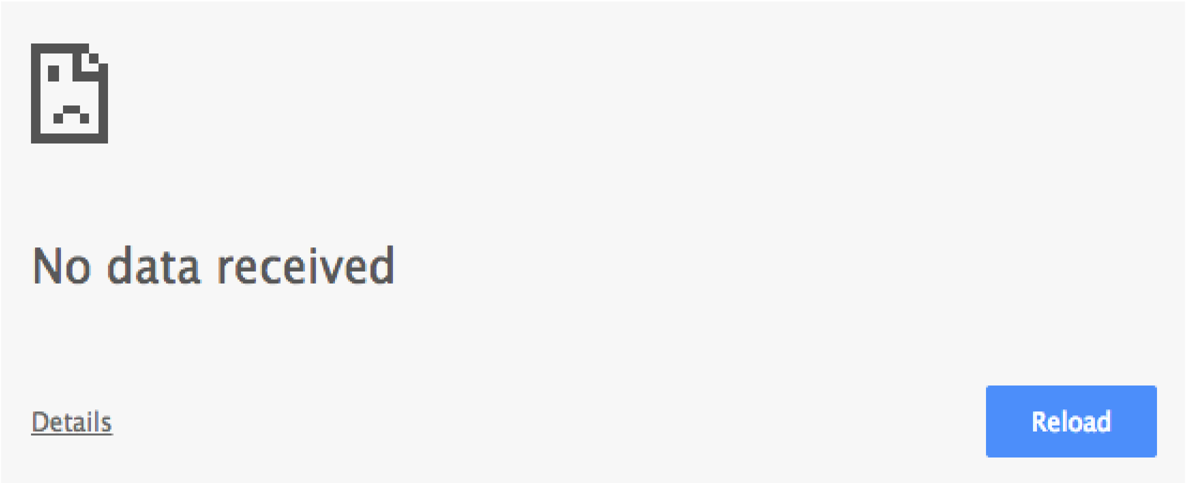
- Toxicity of the chemical alone doesn't determine the risk – nuclear waste sealed in lead barrels
- Exposure to the chemical alone doesn't determine the risk – we drink water everyday
- Risk = exposure * toxicity
- Add in the consideration of released amount, we can assess the impact
- Impact = release (or emission) * risk

Predictive Life Cycle Impact Assessment



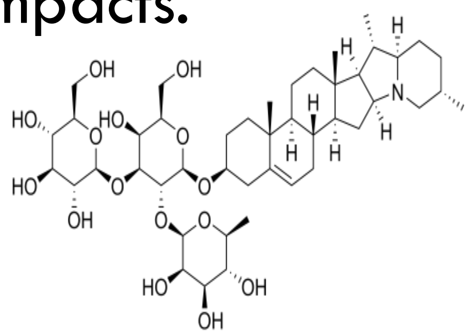
Predictive Life Cycle Impact Assessment

- User might unable to provide key inputs for other modules in CLiCC. Or they are confidential.
- Alternative path to estimate mid-point characterized results (GWP) and end-point characterized results (human health) based on very simple inputs.

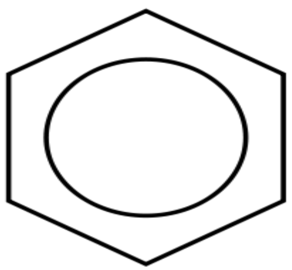


Learning from Molecular Structure

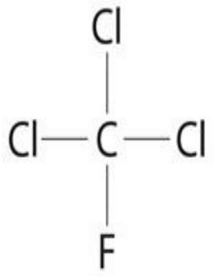
- How do we know the life-cycle impacts with simple inputs?
- Chemical structure is correlated with its properties and impacts.



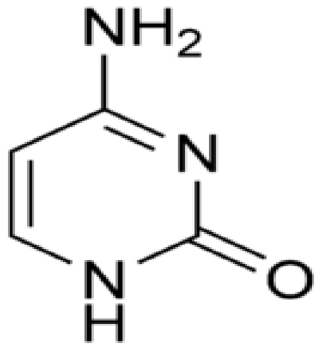
Might consume more energy



…than this



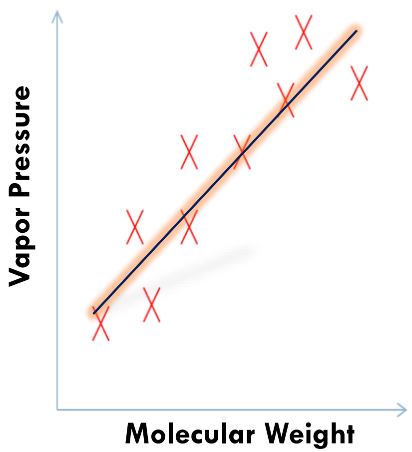
Higher global warming impact

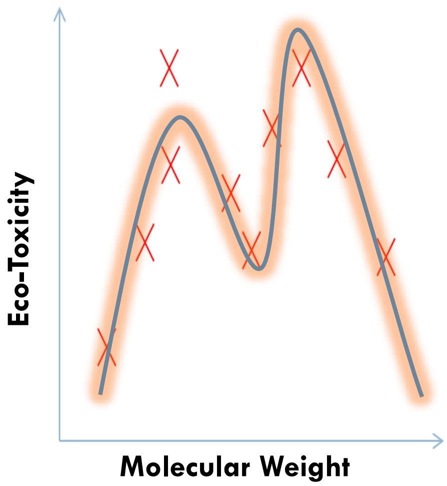


…than this

Learning from Molecular Structure

- Chemical structure can be presented by molecular descriptors. (MW, Num. Carbon…)
- Build regression model to predict the characterized results.

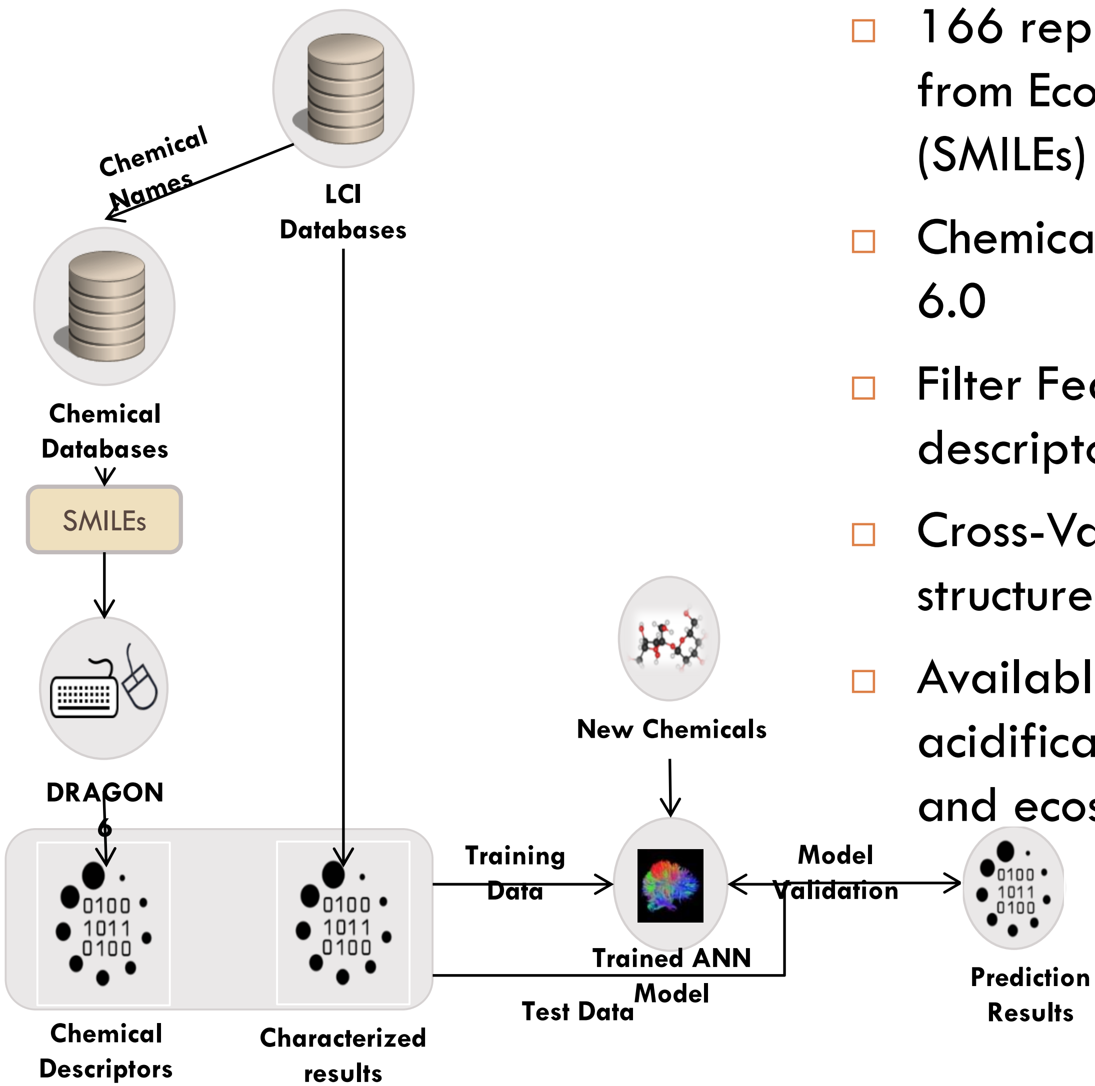




- A Nonlinear regression model: Artificial Neural Network (ANN).
- More complicate than liner regression, better predictive power.

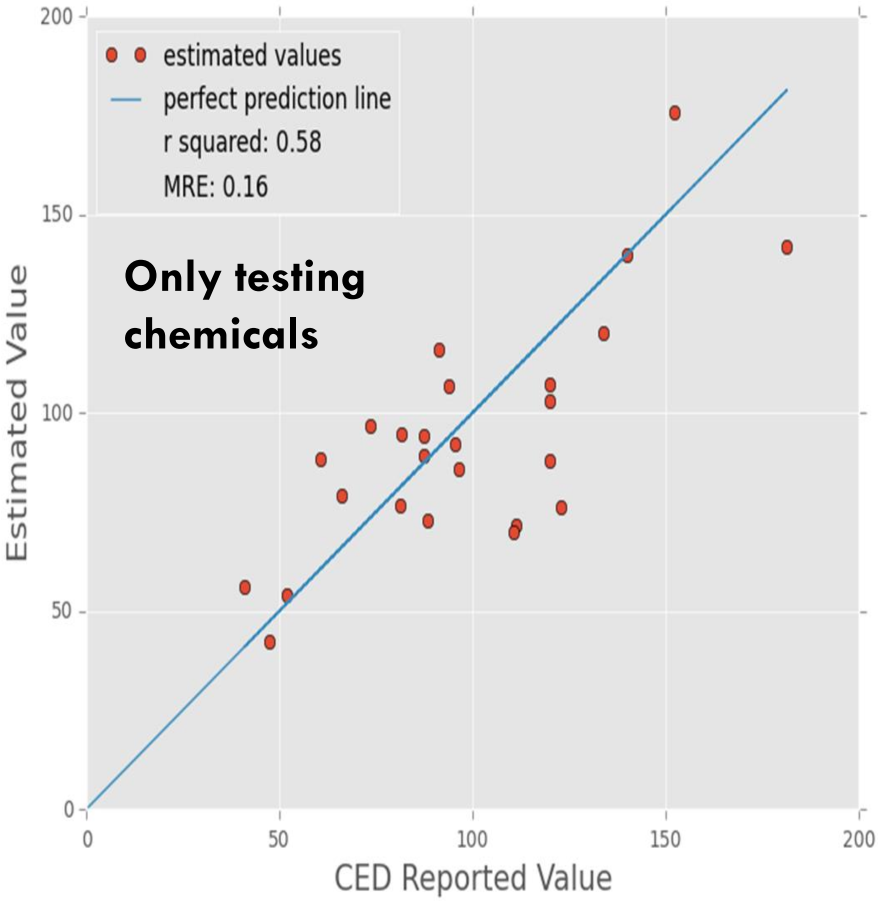
Artificial Neural Networks

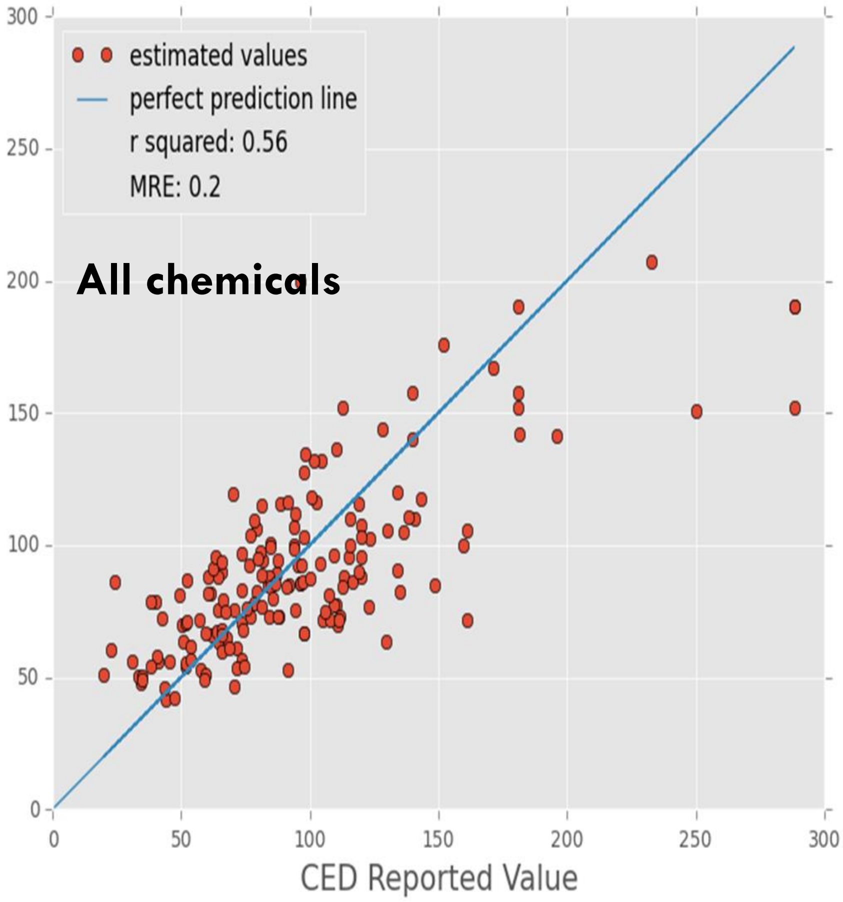
Model Development Procedure



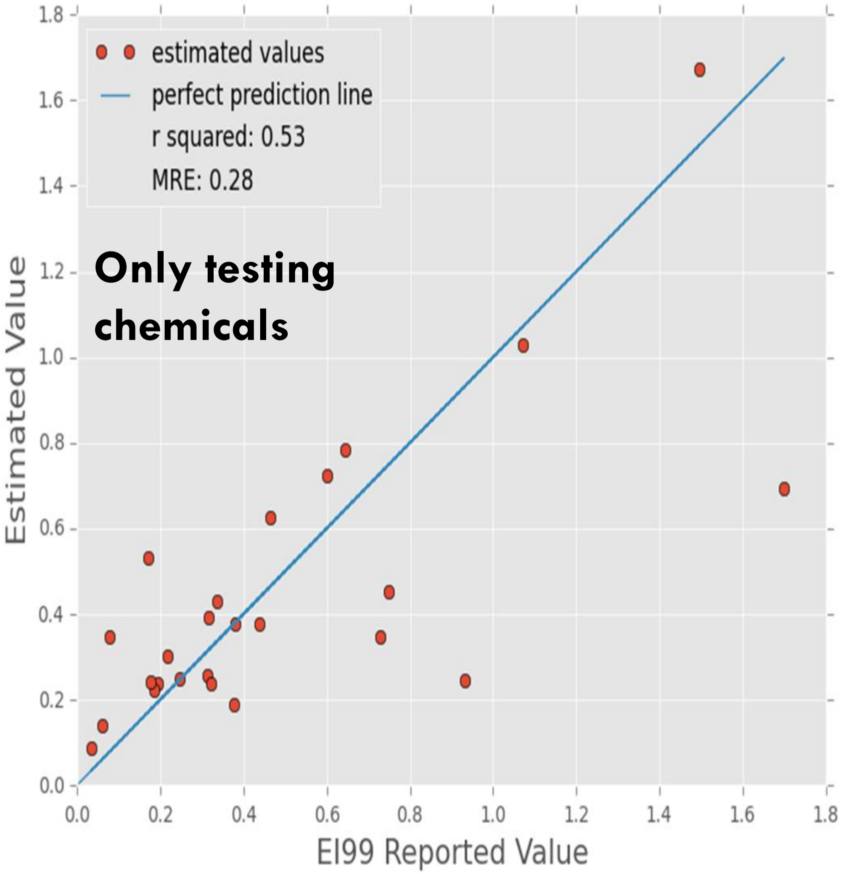
- 166 reported characterized results collected from Ecoinvent 3.01; Chemical Identifier (SMILEs) come from ChemSpider
- Chemical Descriptors calculated by Dragon 6.0
- Filter Feature Selection algorithm reduces descriptors from 4,000 to 30
- Cross-Validation to achieve the best ANN structures
- Available impact categories are: CED, acidification, GWP, human health, ecotoxicity and ecosystem quality.

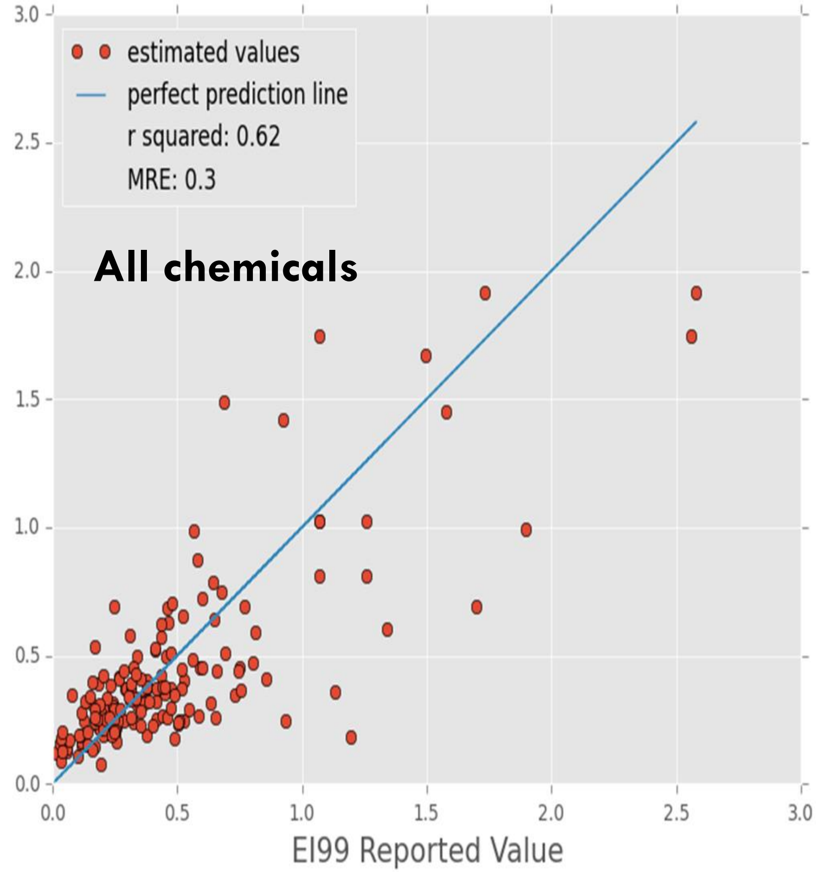
Model Performance -- CED





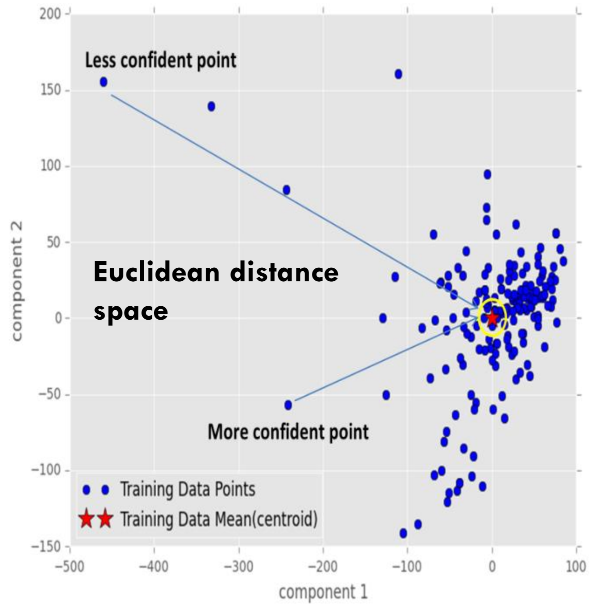
Model Performance – EI99

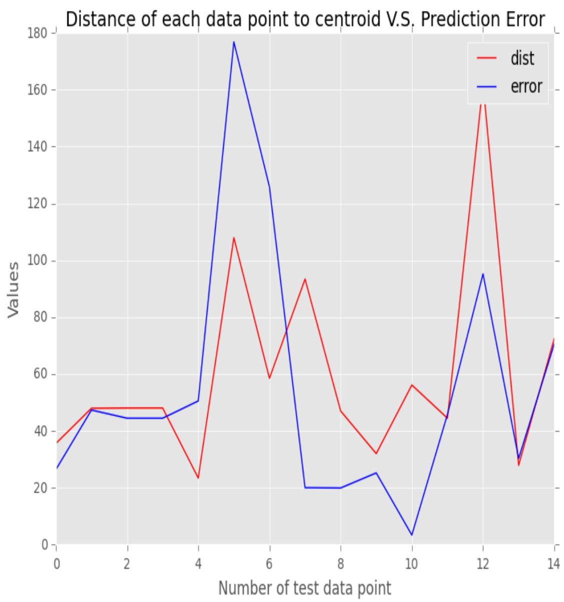




Model Applicable Domain

- Query chemicals that have higher structural similarity with the training data are likely to have higher prediction accuracy.
- Accuracy could be measured depending on if this chemical falls into the applicable domain.





Model Applicable Domain

Model	Selected Cut-off Threshold	MRE inside AD	MRE outside AD	Sample Size inside AD	Sample Size outside AD
CED	100	14%	26%	23	2
Eco-Indicator	60	23%	35%	4	21
Acidification	110	21%	46%	21	4
GWP	100	48%	89%	19	6
Human Health	90	40%	60%	16	8
Ecosystem Quality	60	49%	82%	7	17

Conclusions & Future Outlooks

- We developed a model to screening chemical life-cycle impact using molecular structure information.
- Three mid-points and three end-points impact categories are available at this point.
- Model applicable are characterized.

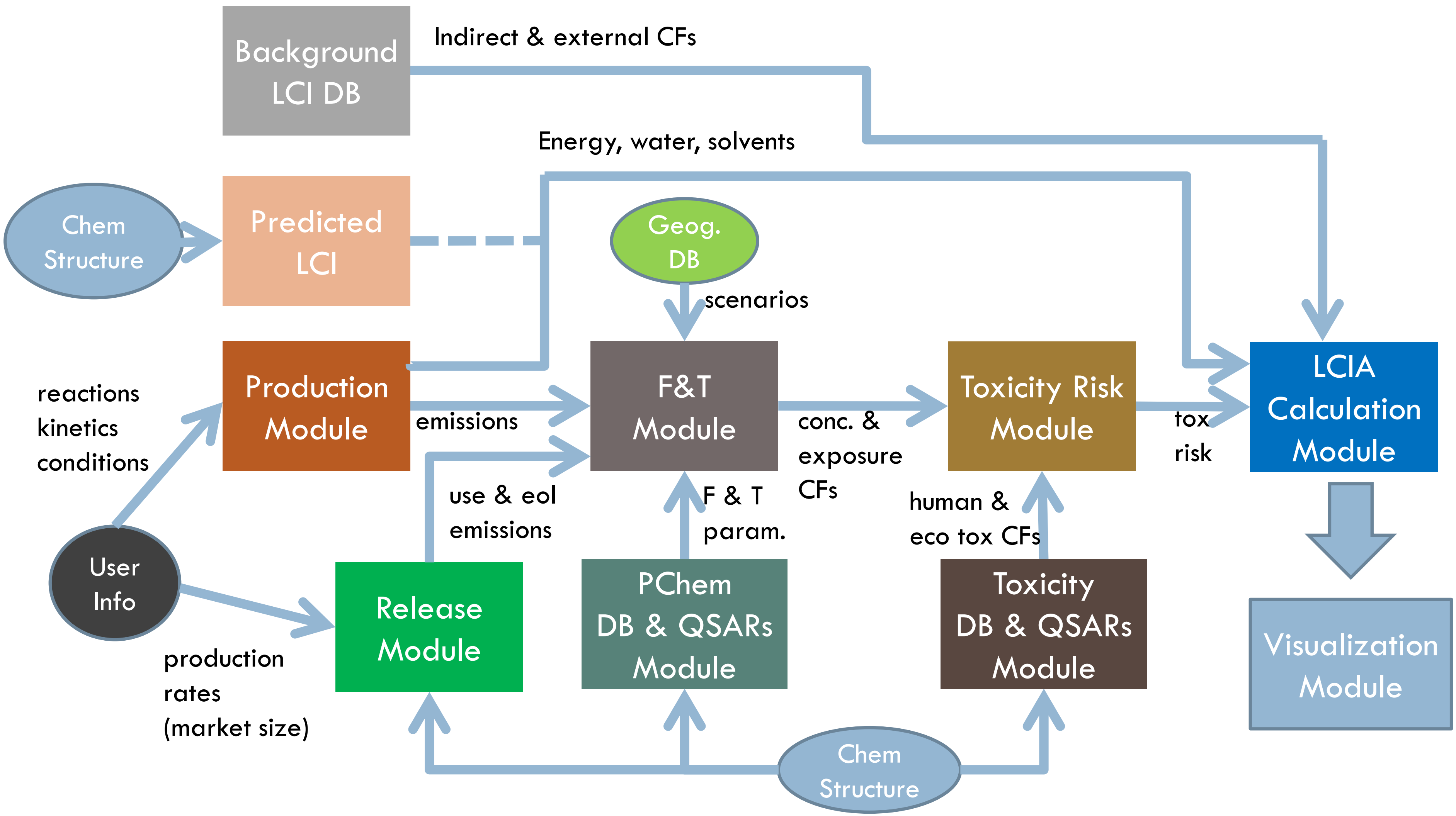
- Increase the number of predictable impact categories.
- Collect more chemical LCI data as training dataset.

Uncertainty Module

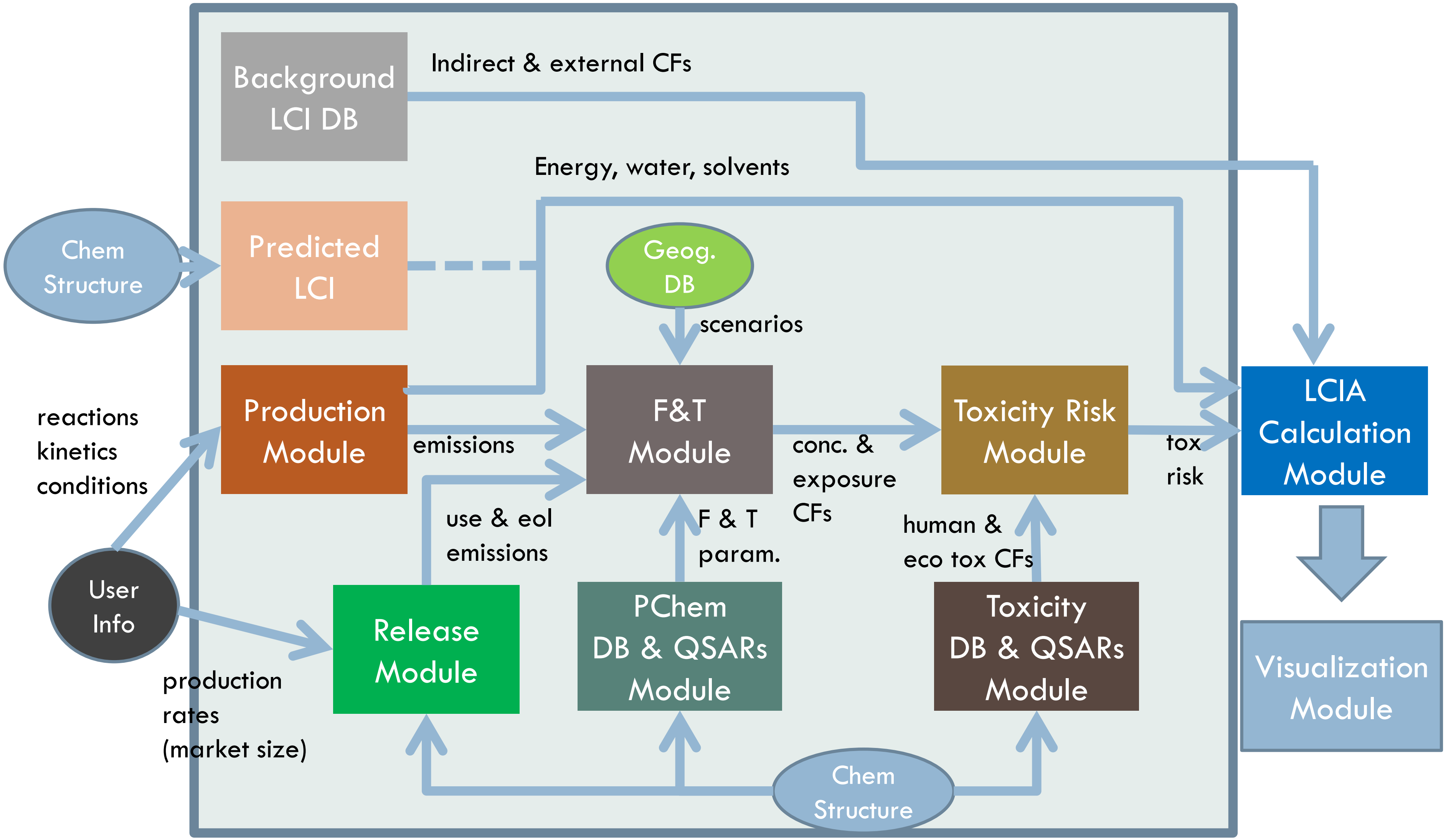
Yuwei Qin

yqin@bren.ucsb.edu

Uncertainty



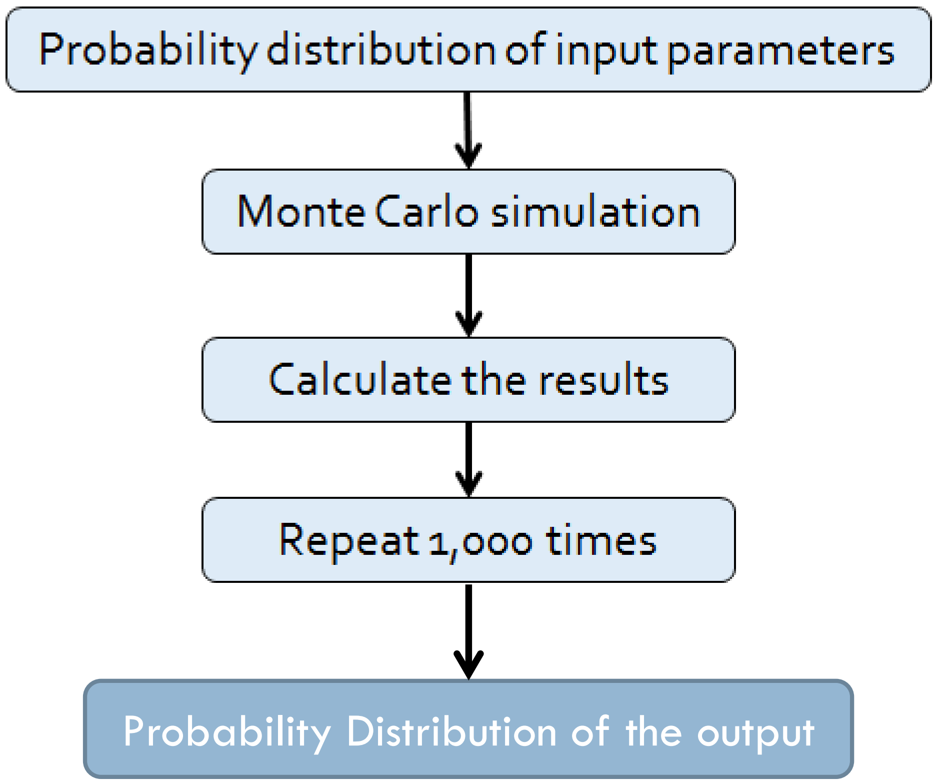
Uncertainty

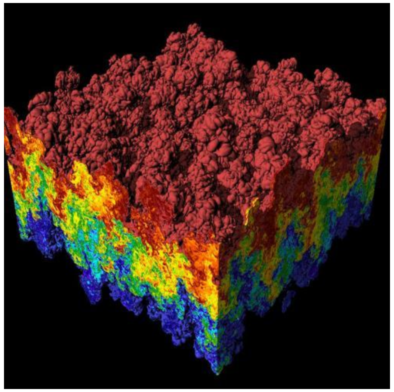


Uncertainties - How to treat them?

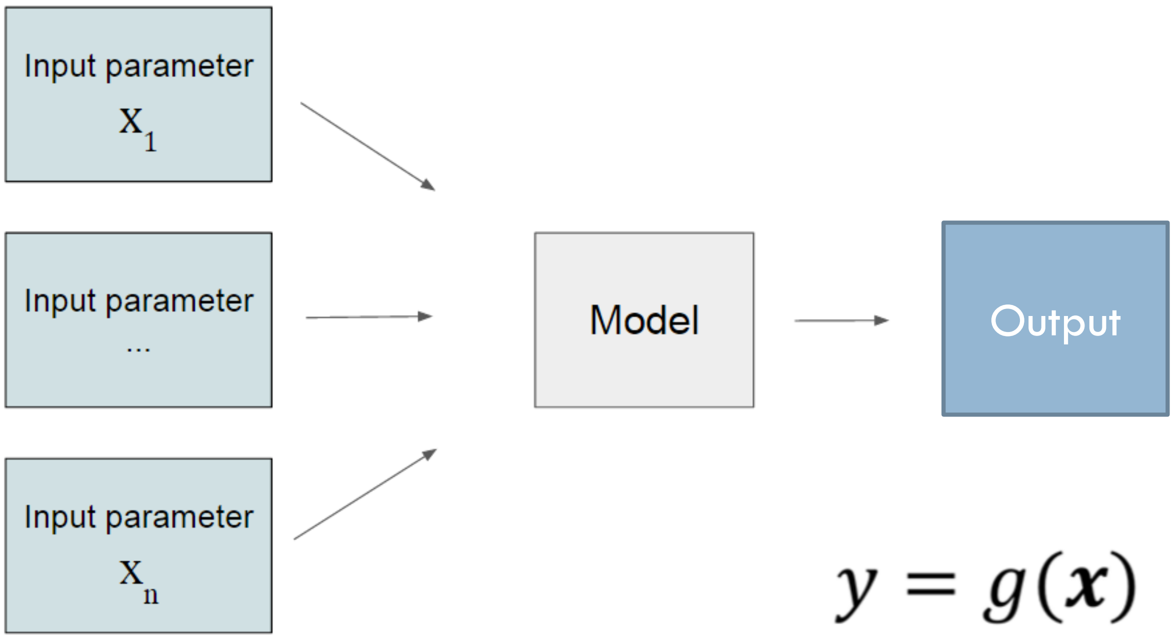
- Collect data
- Estimate a distribution or uncertainty range for each input
- Apply Monte Carlo method or similar tools to simulate uncertainty
- Alternative approach: analytical solutions

Uncertainty – Monte Carlo simulation



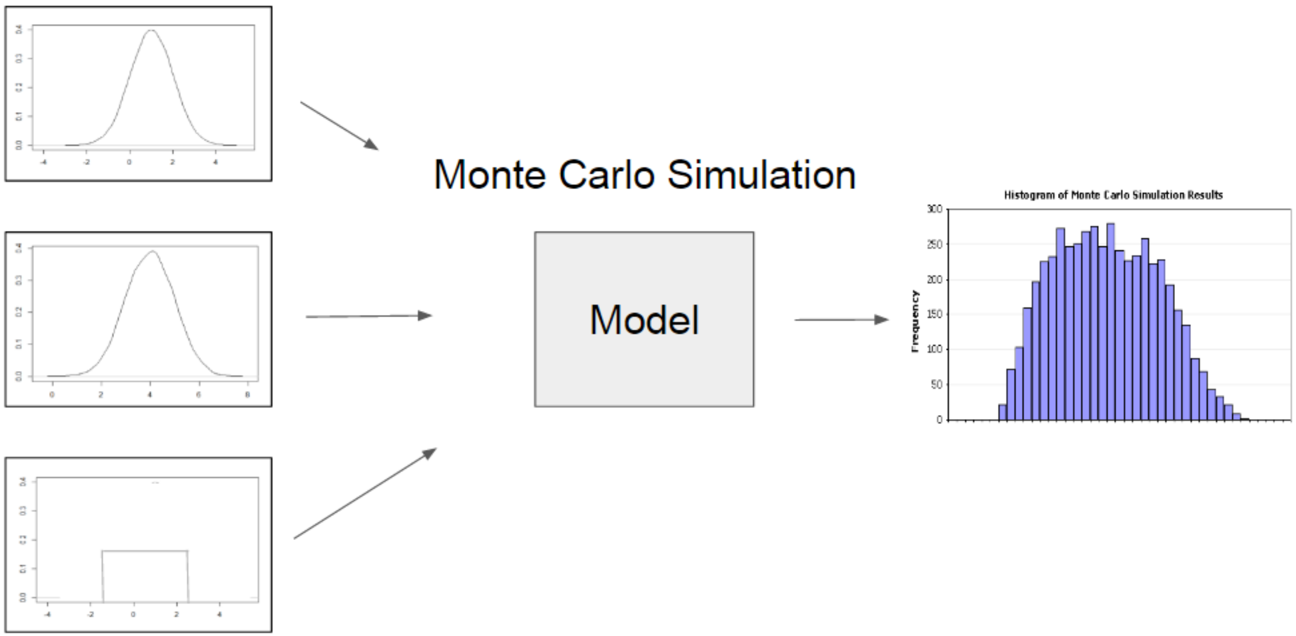


Uncertainty – A conceptual model



$$y = g(\boldsymbol{x})$$

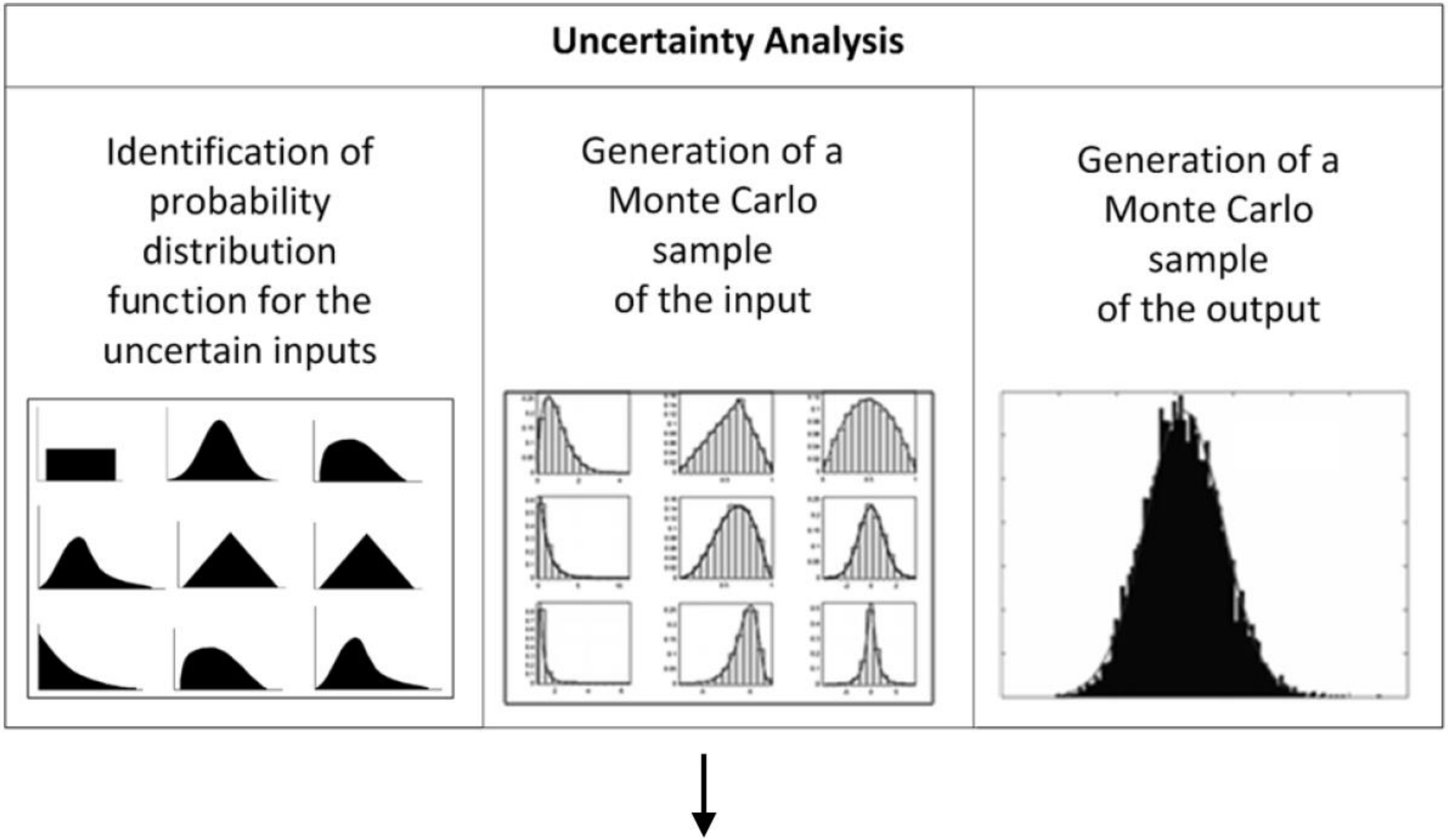
Uncertainty- A model with uncertain parameters



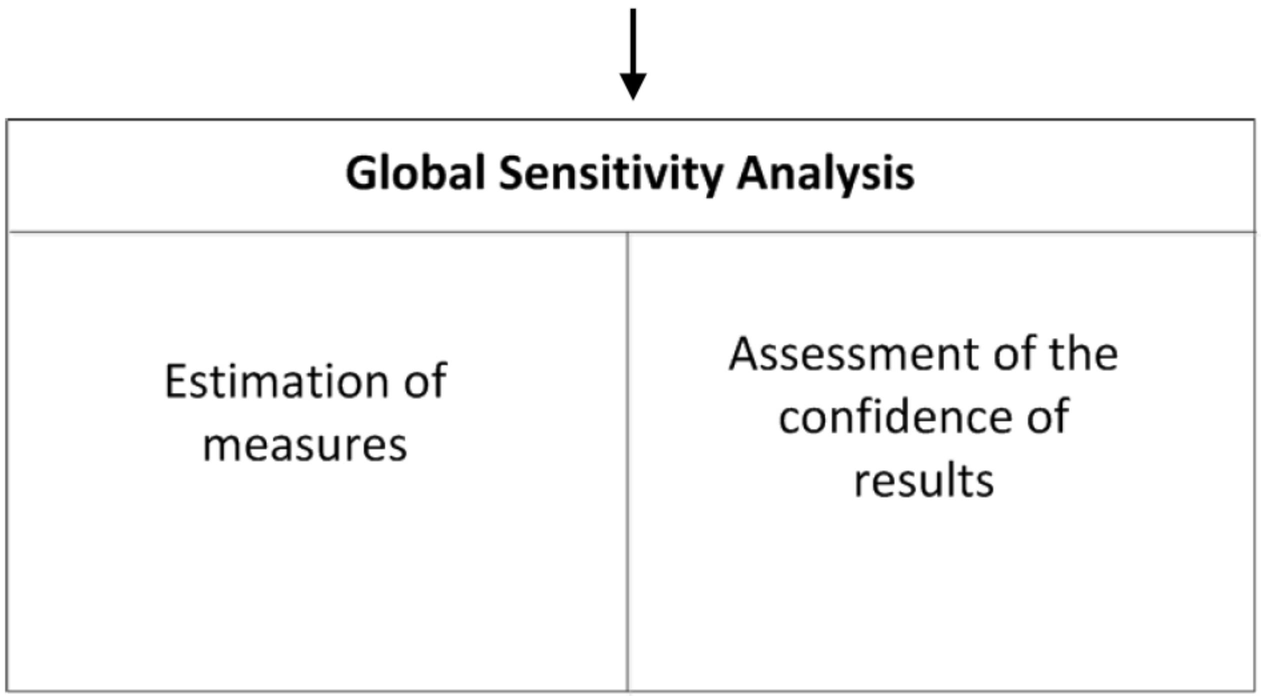
Global Sensitivity Analysis

- To understand the model structure and the input-output relationships
- To identify major contributors to output uncertainty in the uncertain inputs space
- We use a global approach, varying all inputs simultaneously considering their full distribution

We perform them jointly

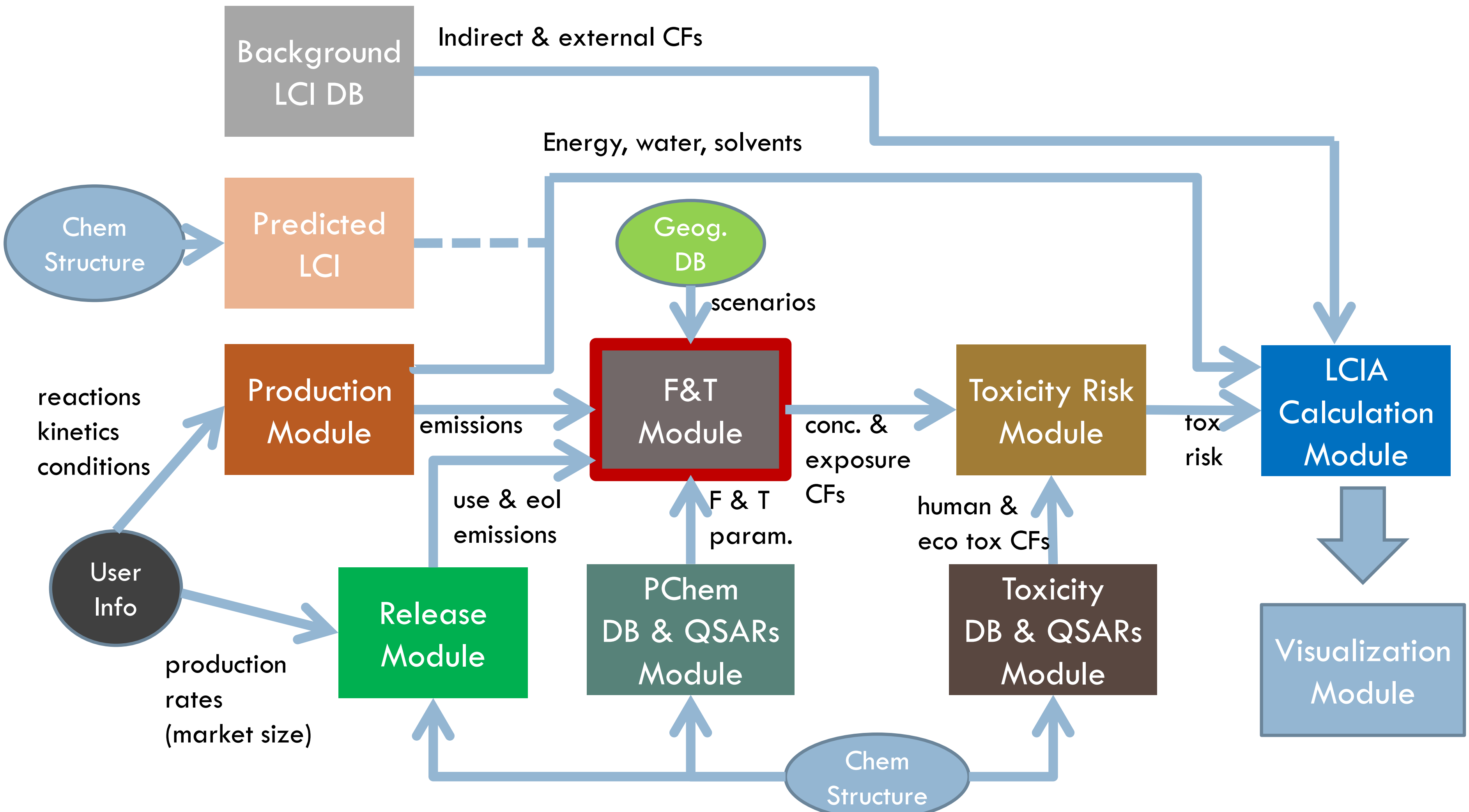


Joint uncertainty and sensitivity analysis

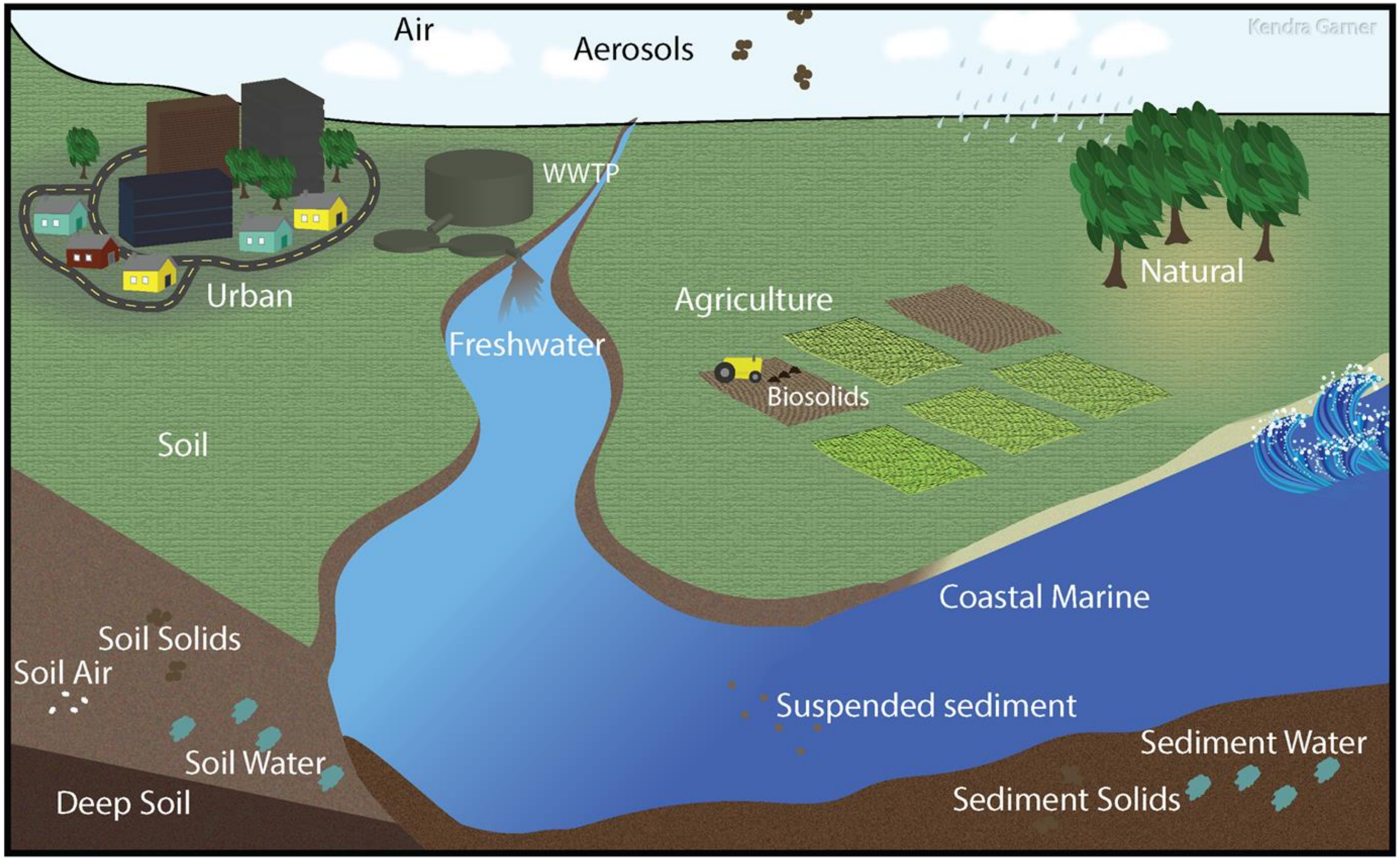


SAME MC SAMPLE!

Uncertainty – Applied to the Fate and Transport model



Uncertainty – Applied to the Fate and Transport model

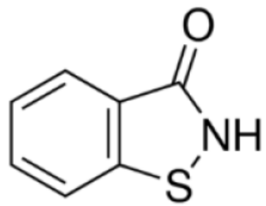


Uncertainty – Model inputs

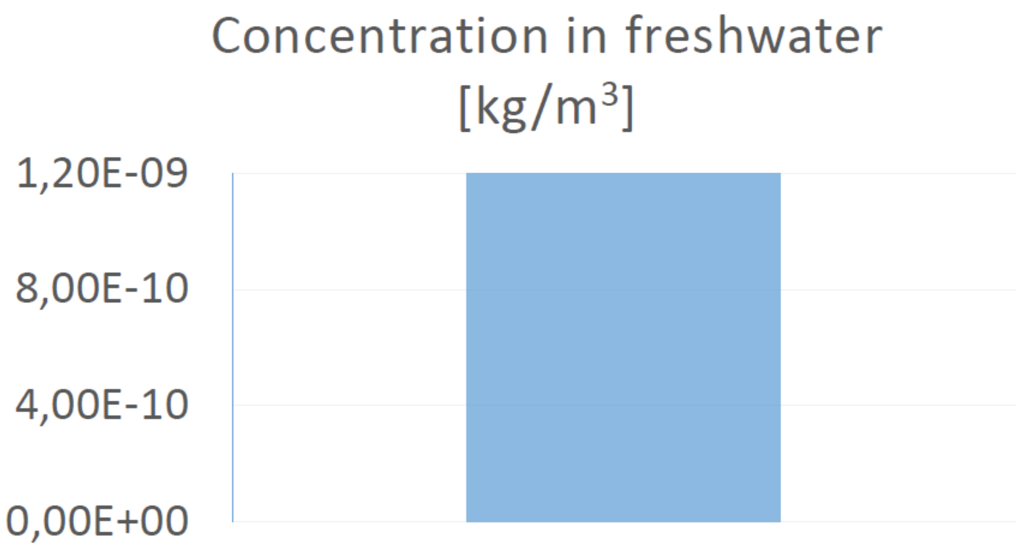
- Meteorological Data (e.g. precipitation, temperature)
- Water (e.g. pH, salinity)
- Soil (e.g. soil type, land use)
- Chemical Characteristics (e.g. half-life from QSARs)

Uncertainty – Model output

Benzisothiazolone

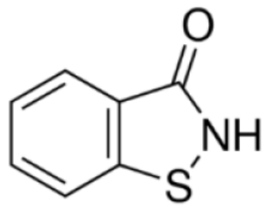


CAS # 2634-33-5

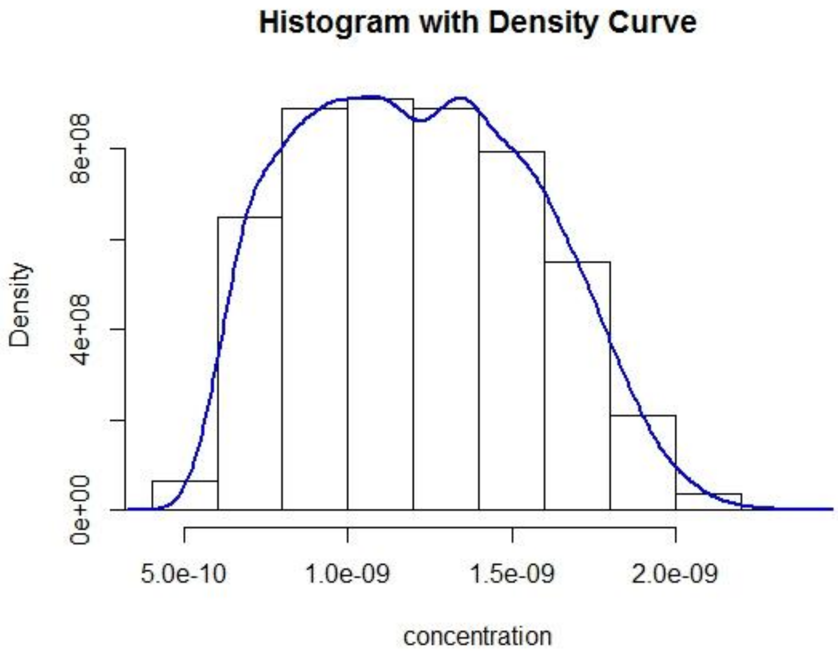


Uncertainty – Results for the concentration in freshwater

Benzisothiazolone

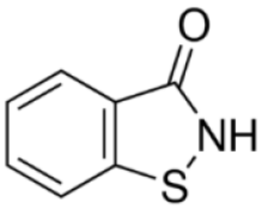


CAS # 2634-33-5



Uncertainty – Other ways to communicate uncertainty

Benzisothiazolone

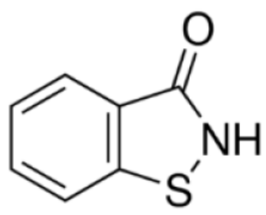


CAS # 2634-33-5

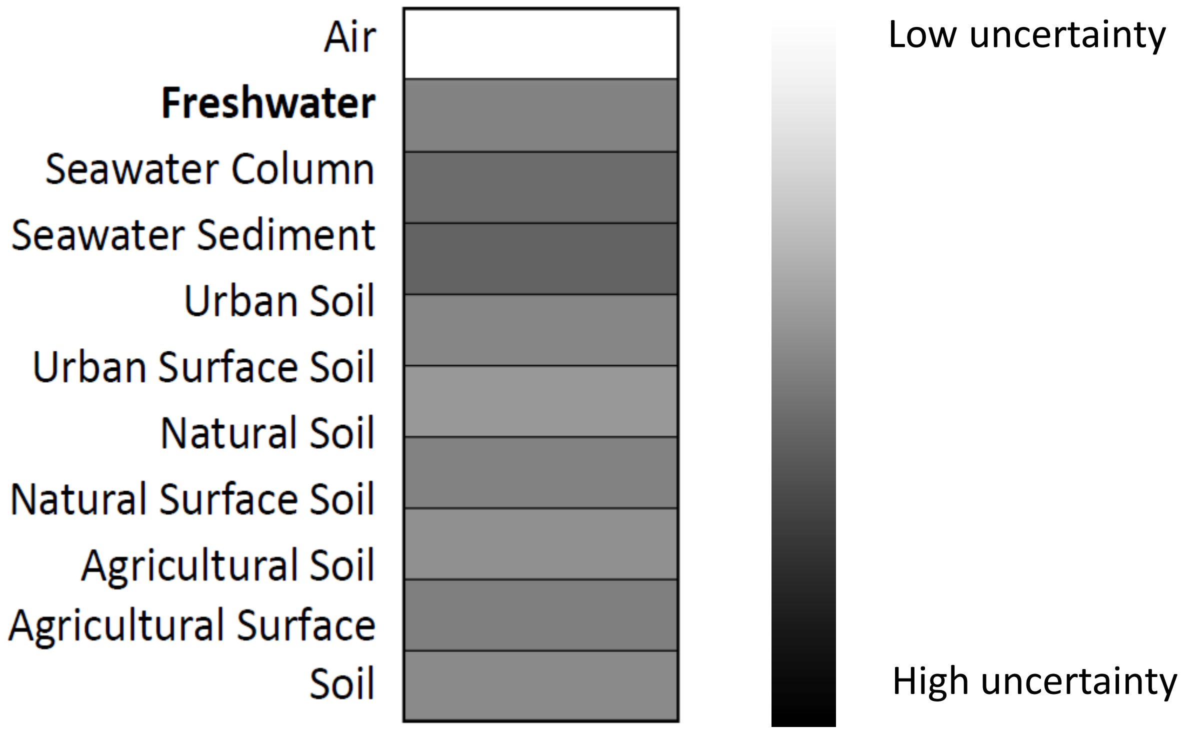
Concentration in freshwater	
Deterministic [kg/m^3]	1.20E-09
Probabilistic average [kg/m^3]	1.21E-09
Probabilistic median [kg/m^3]	1.20E-09
Coefficient of variance	0.29
k-value (Slob, 1994)	1.73
k-value (Nunez et al., 2015)	1.28

Uncertainty – Other ways to communicate uncertainty

Benzisothiazolone

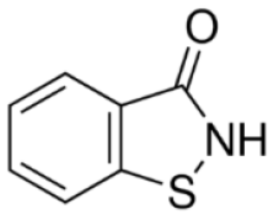


CAS # 2634-33-5



Global Sensitivity analysis

Benzisothiazolone

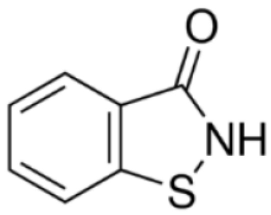


CAS # 2634-33-5

Importance ranking	Input
1	Degradation rate in water
2	Air/water partition coefficient
3	Depth freshwater
4	Natural soil area
5	Degradation rate in air (half-life)
…	…
101	…

Global Sensitivity analysis

Benzisothiazolone



CAS # 2634-33-5

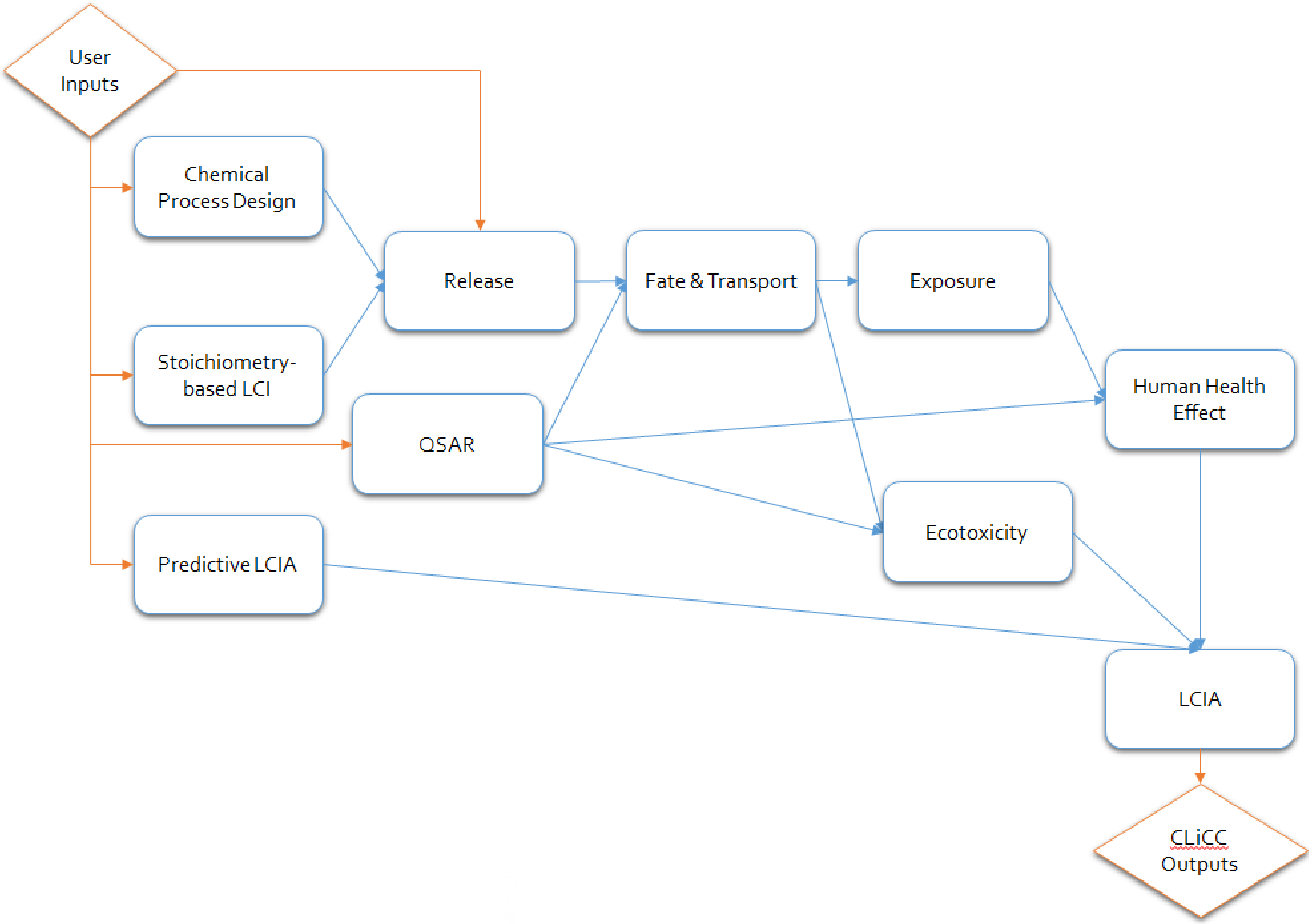
Importance ranking	Input
1	Degradation rate in water
2	Air/water partition coefficient
3	Depth freshwater
4	Natural soil area
5	Degradation rate in air (half-life)
…	…
101	…

>95%

We provide users with a complete set of information together with the results

- About the input-output relationships
- About the output distribution
- About the major contributors to the output uncertainty
- Default uncertainty values can be updated by the user if better information is available

Application of CLiCC



Industry Partners

3M

american cleaning institute
for better living
aci

California Department of
Toxic Substances Control

DOW

ECOLAB

FCh
FUNDACIÓN CHILE

Henkel

Nestlé

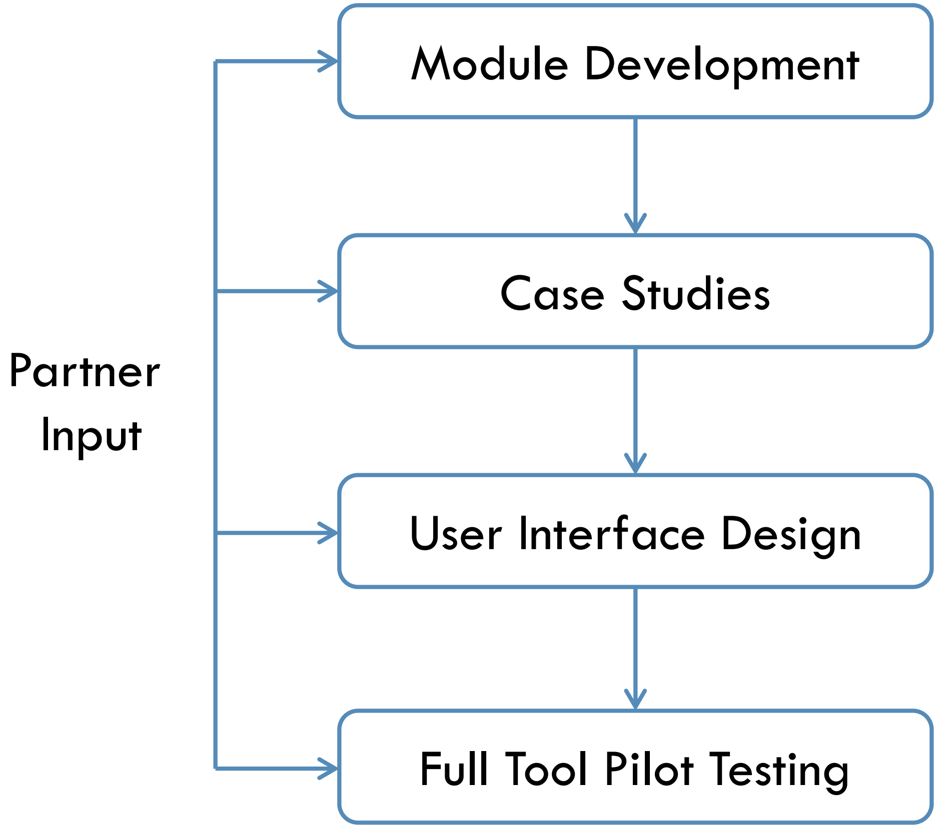
SHERWIN WILLIAMS.

SINOPEC
中国石化

Sustainable
Apparel Coalition

Unilever

Stakeholder Engagement



Project Benefits

- design guided by user needs -

- validate with industry data -

- comparison to existing methods -

- establish credibility with users -

What is a case study?

- A test case for the CLiCC tool using inputs/data from an industry partner
- Can include all the tool's modules or an isolated combination of several modules
- Can analyze one chemical, a group of chemicals, or an entire product with the chemical formulation

Case Study Design

CLiCC goal

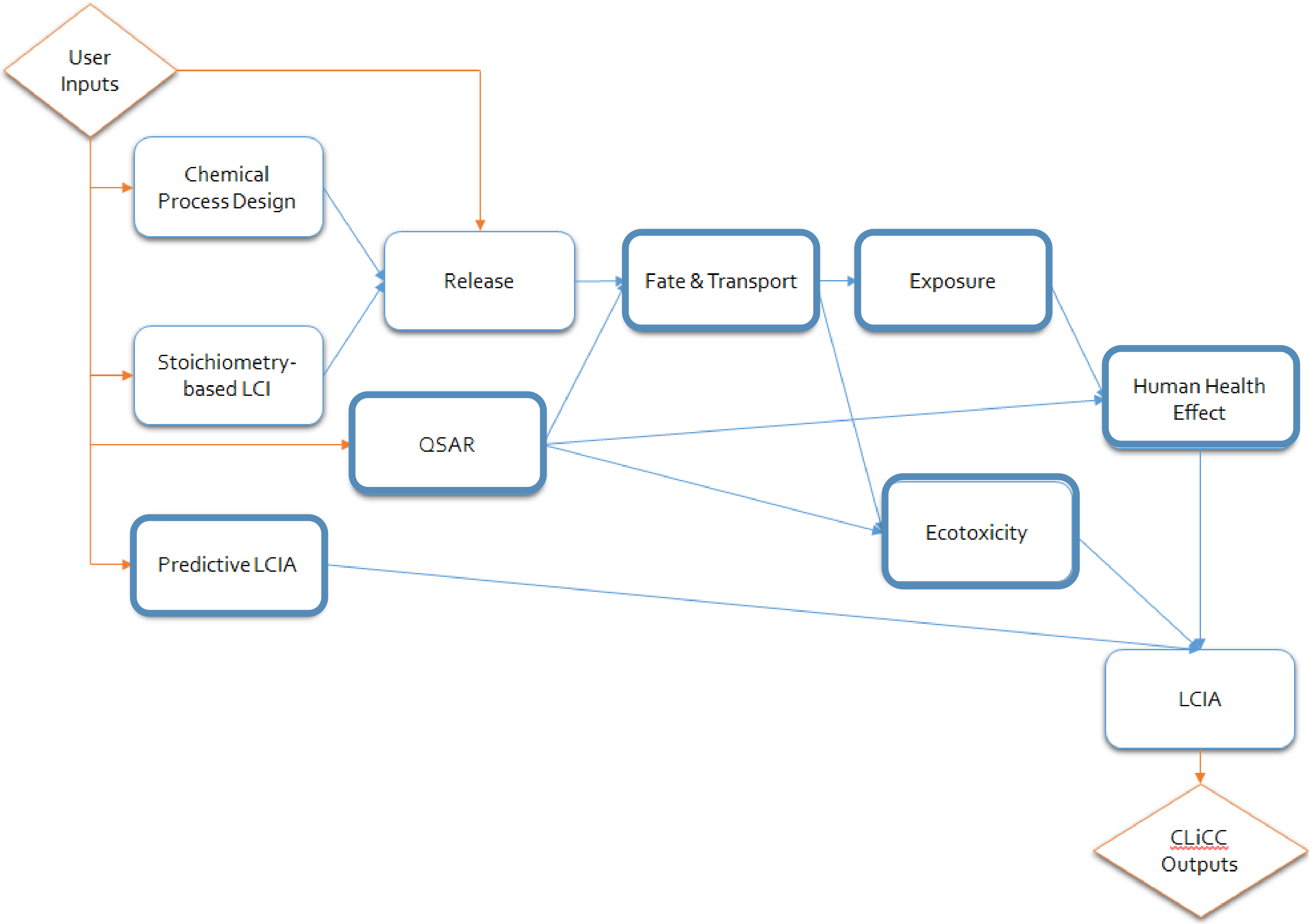
- Validate models
- Test feasibility & limitations
- Understand user preferences
  - inputs and outputs

Industry Partner goal is defined when setting scope and outlining case study

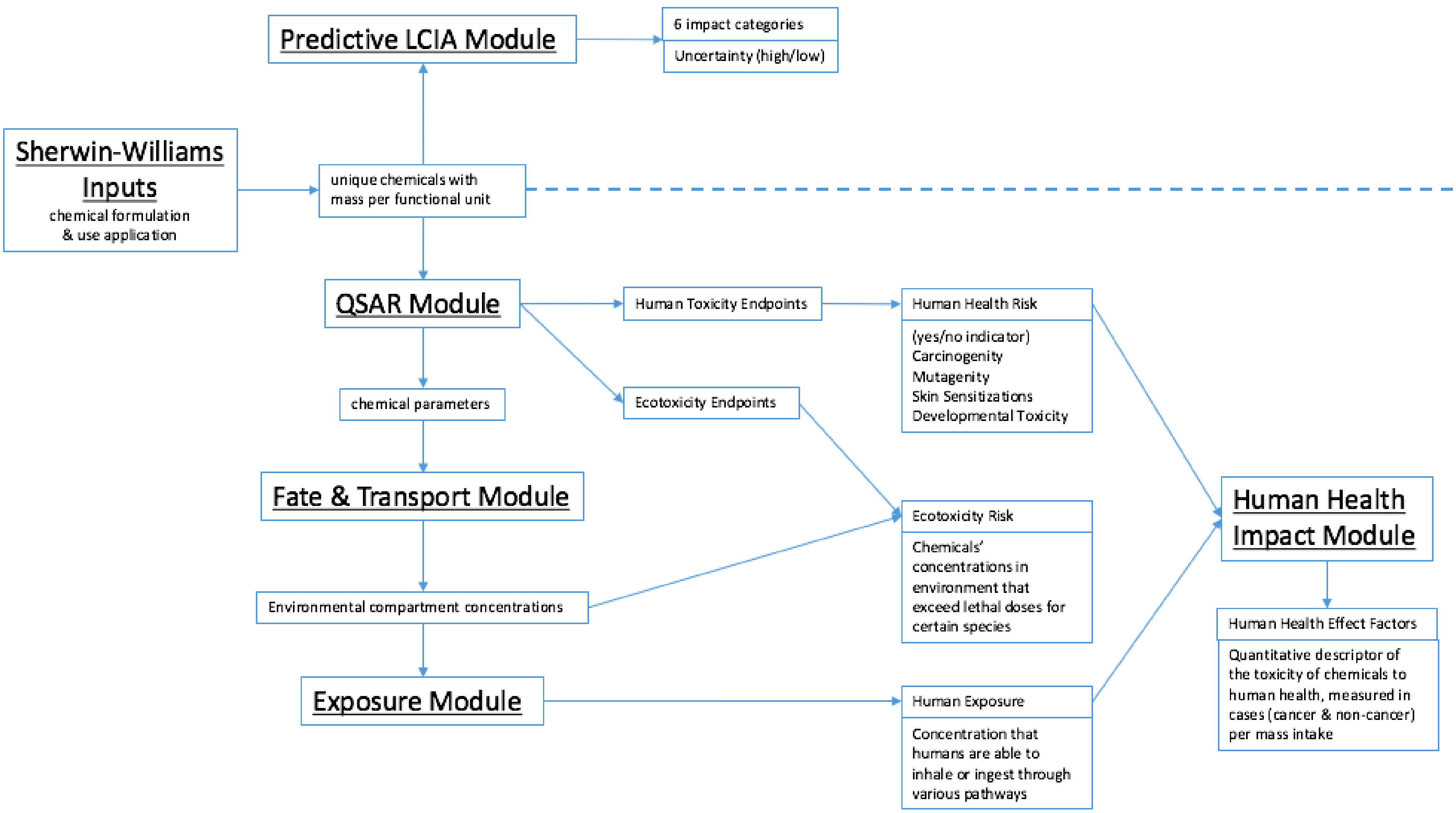
Case Study Example

Industry Partner	Sherwin-Williams
Product Type	Interior Paint (coating)
Release Assumptions	(1) To WWTP from brush washing (2) To interior air after application

Sherwin-Williams Case Study Scope



Input/Output Module Flow



Upstream Impacts

Cumulative Energy Demand

Water Demand

Ecotoxicity

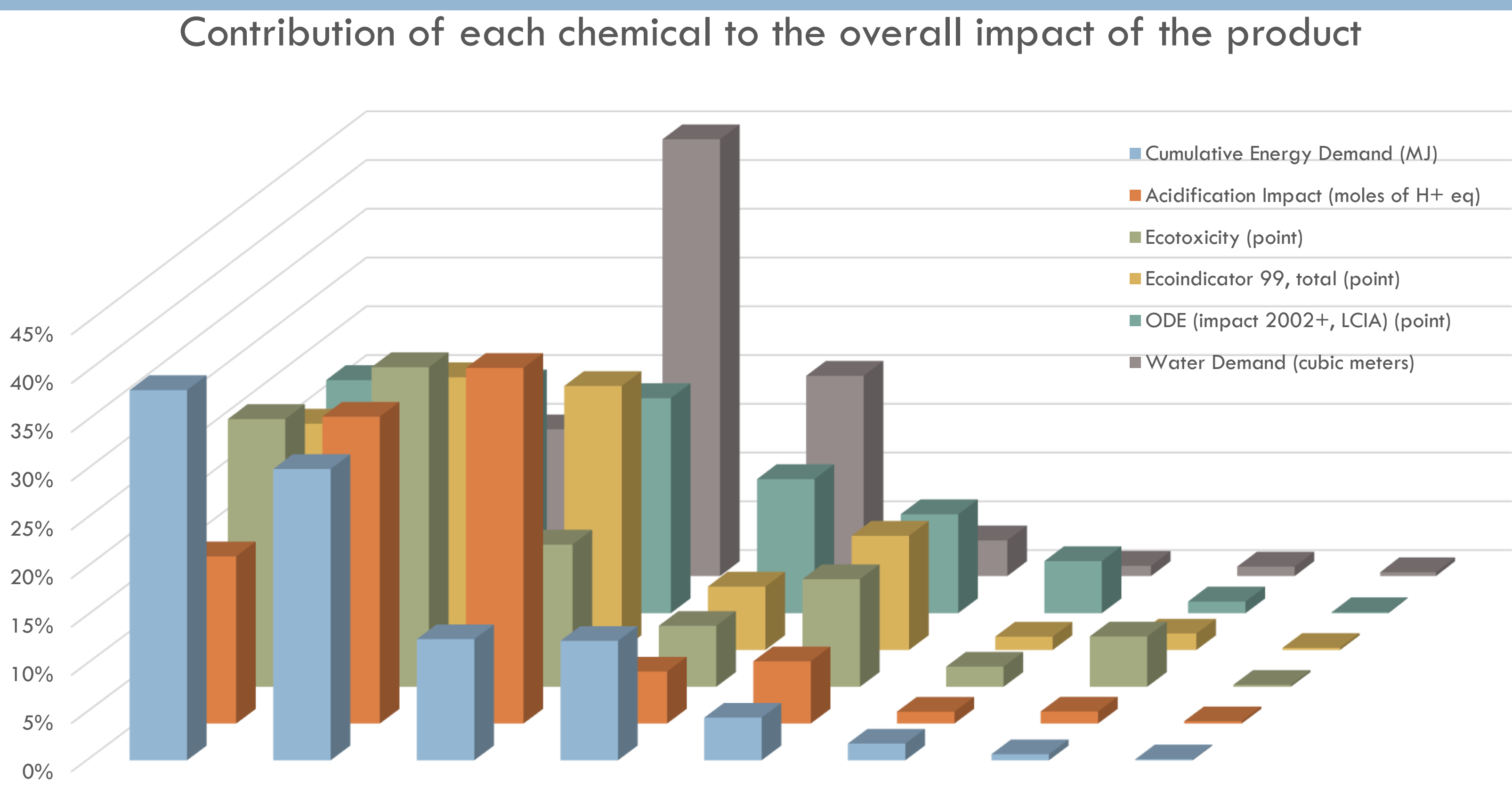
Acidification Impact

Ecoindicator 99, total

ODE (impact 2002+, LCIA)

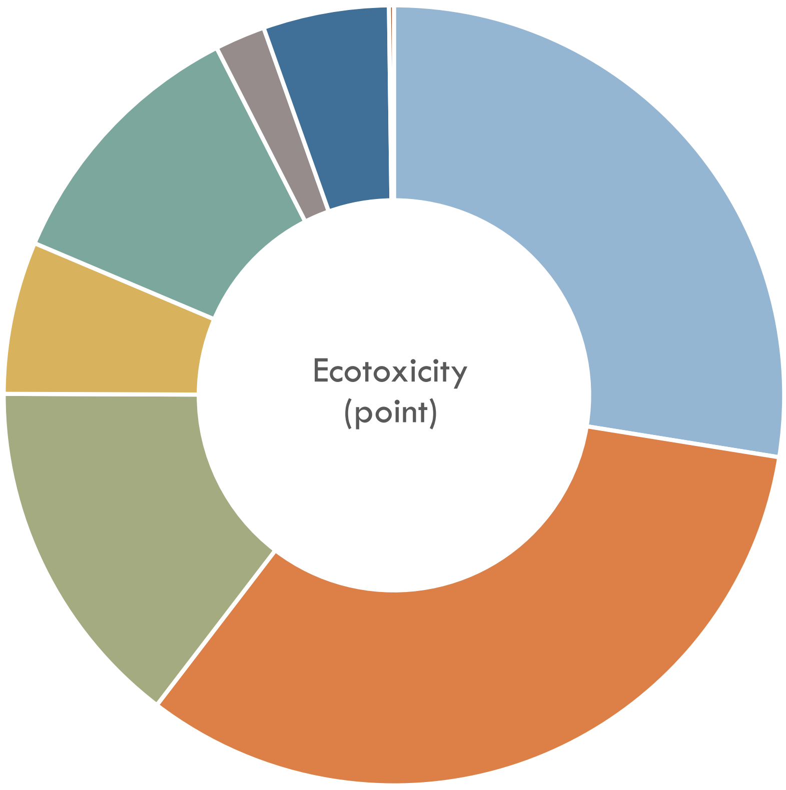
Uncertainty is presented as a "low" (within 30% of actual value) or "high" value

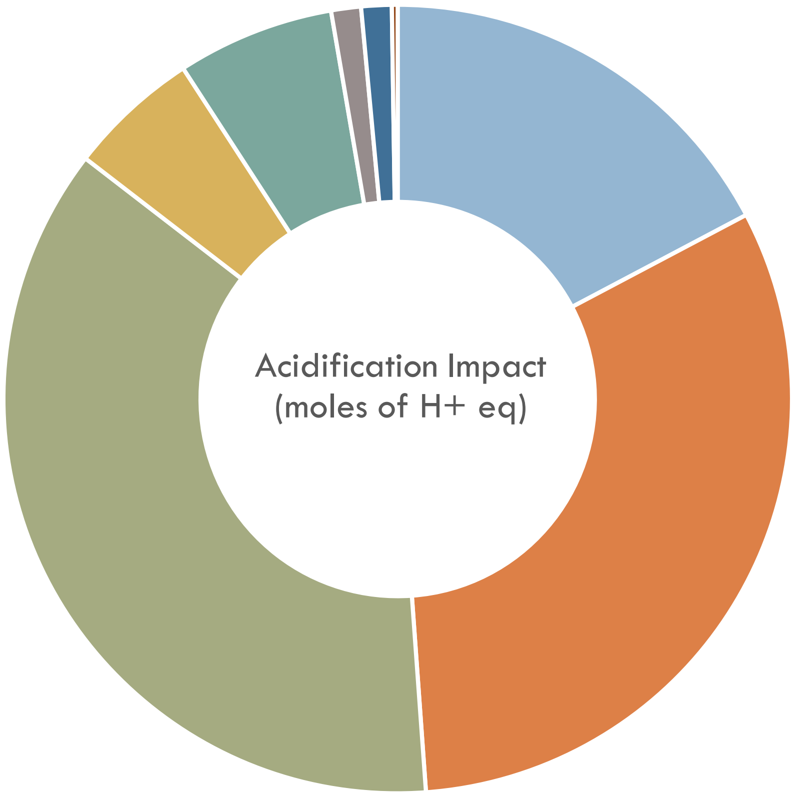
Upstream Impacts – Sample Results



* Y-axis labeled with chemical ingredients. Removed for SW confidentiality purposes.

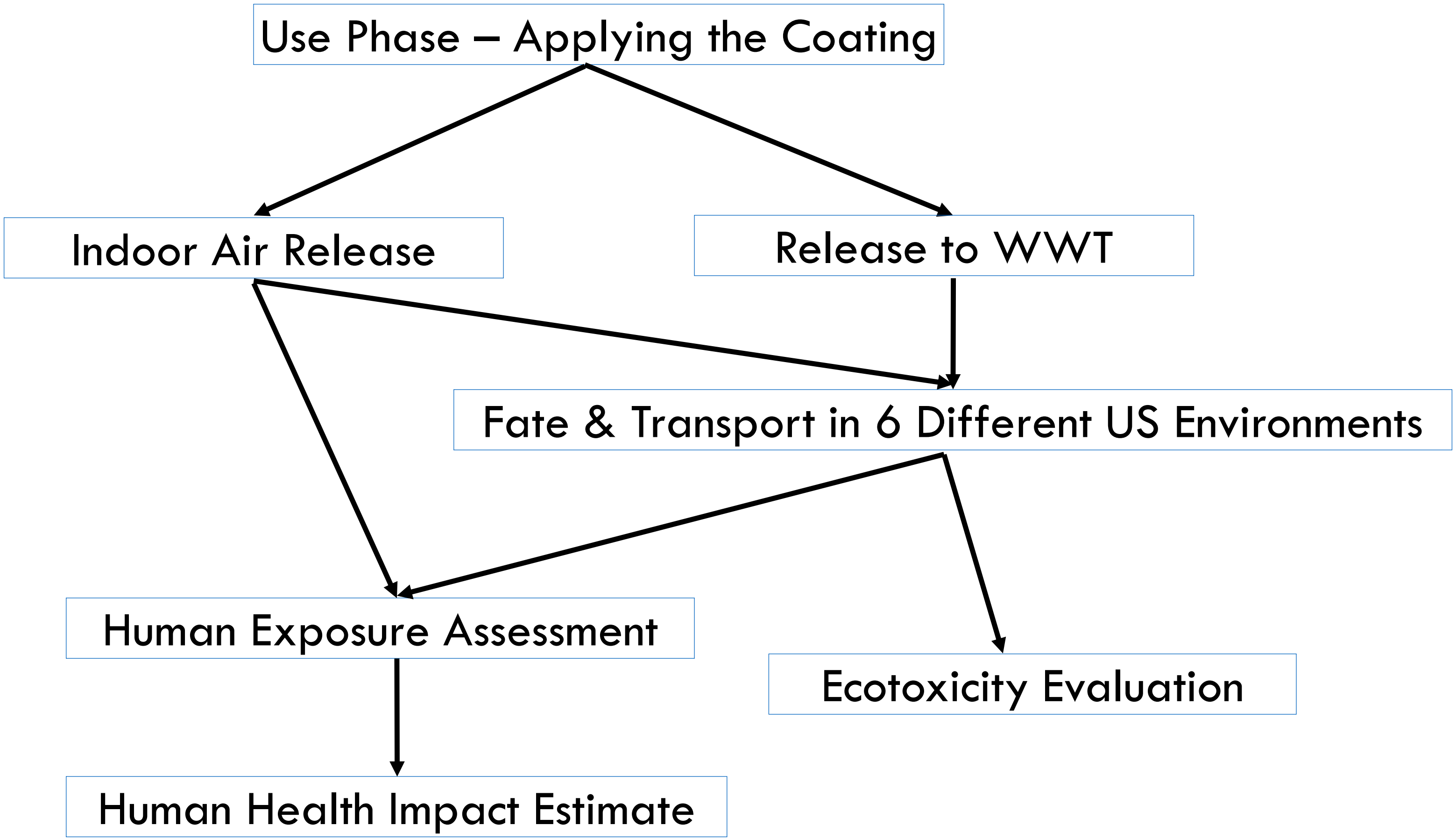
Contribution to each impact category





* Each color represents a different chemical. Labels removed for SW confidentiality purposes.

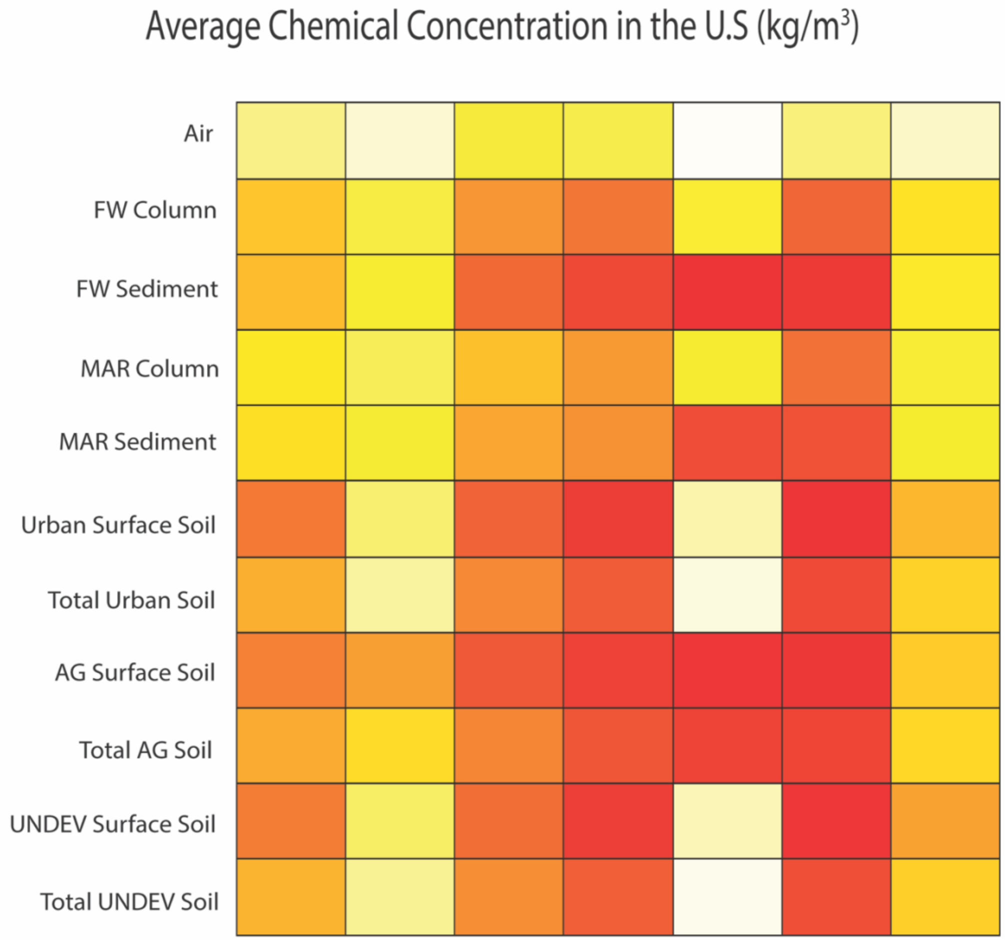
Downstream Impacts



Fate & Transport Results

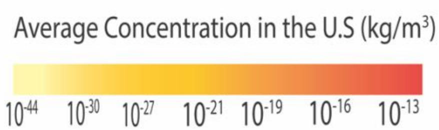
Average Concentration in the U.S (kg/m³) of chemicals in environmental compartments. Value is calculated as the average concentration of a chemical across six locations - Los Angeles, CA; , San Francisco, CA; Salem, OR; New York City, NY; Des Moines, IA.

FW: Freshwater; MAR: Marine water; URBAN: Urban Soil; UNDEV: Undeveloped Soil; AG: Agricultural Soil



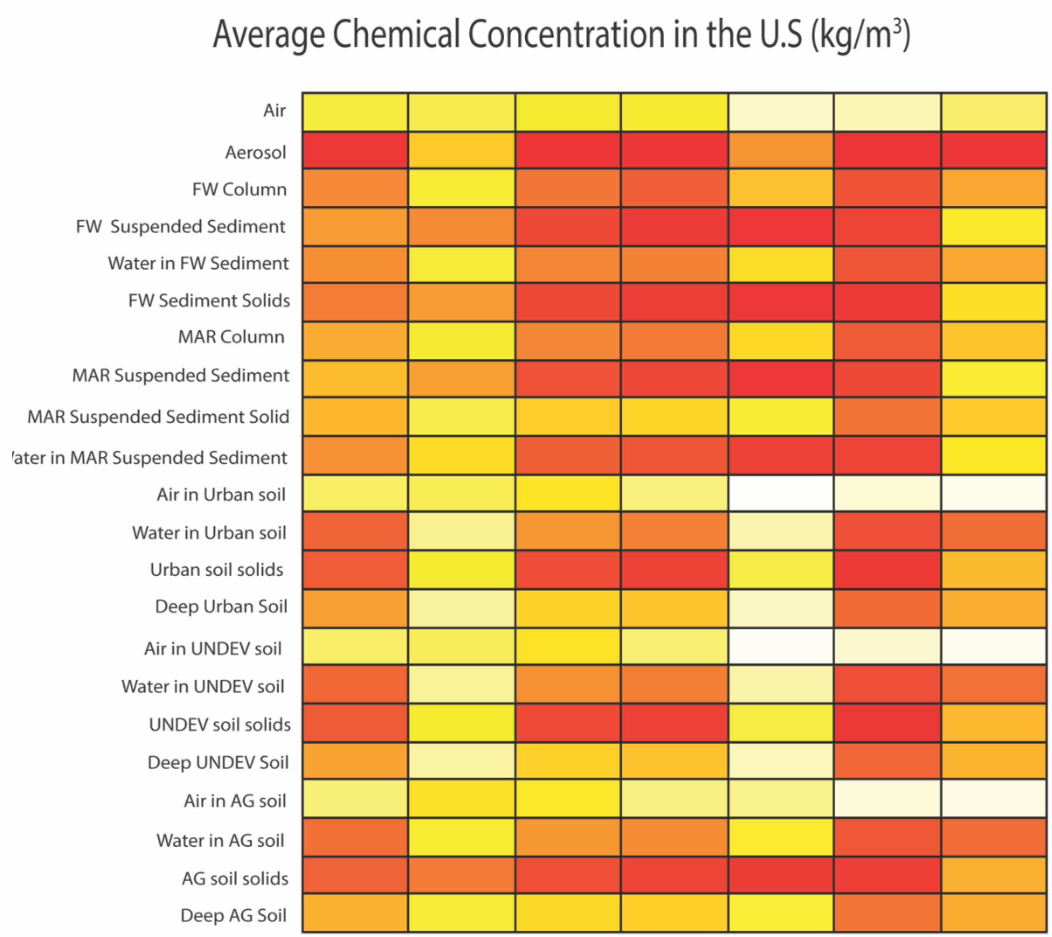
*labels removed for SW confidentiality

Fate & Transport Results



Average Concentration in the U.S (kg/m^3) of chemicals in environmental compartments. Value is calculated as the average concentration of a chemical across six locations - Los Angeles, CA; San Francisco, CA; Salem, OR; New York City, NY; Des Moines, IA.

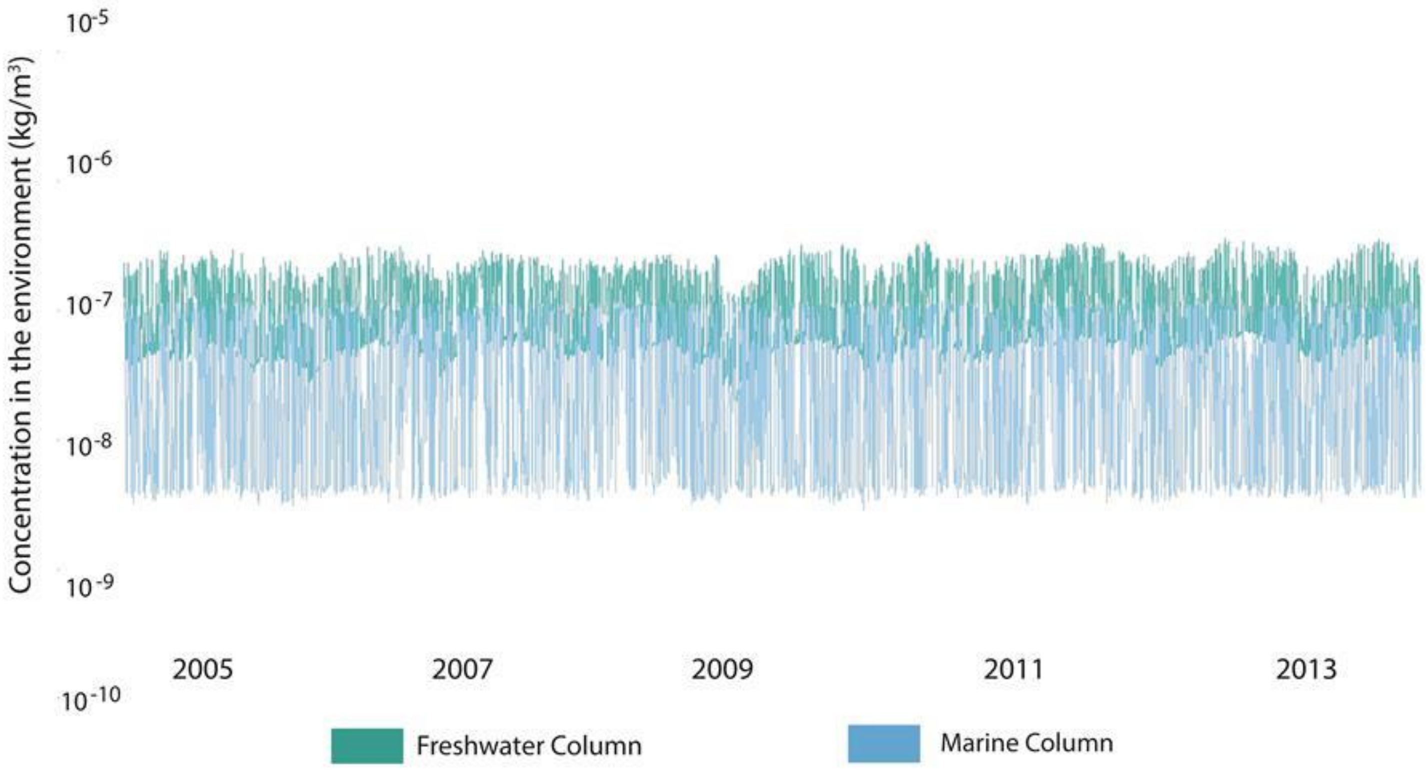
FW: Freshwater; MAR: Marine water; URBAN: Urban Soil; UNDEV: Undeveloped Soil; AG: Agricultural Soil



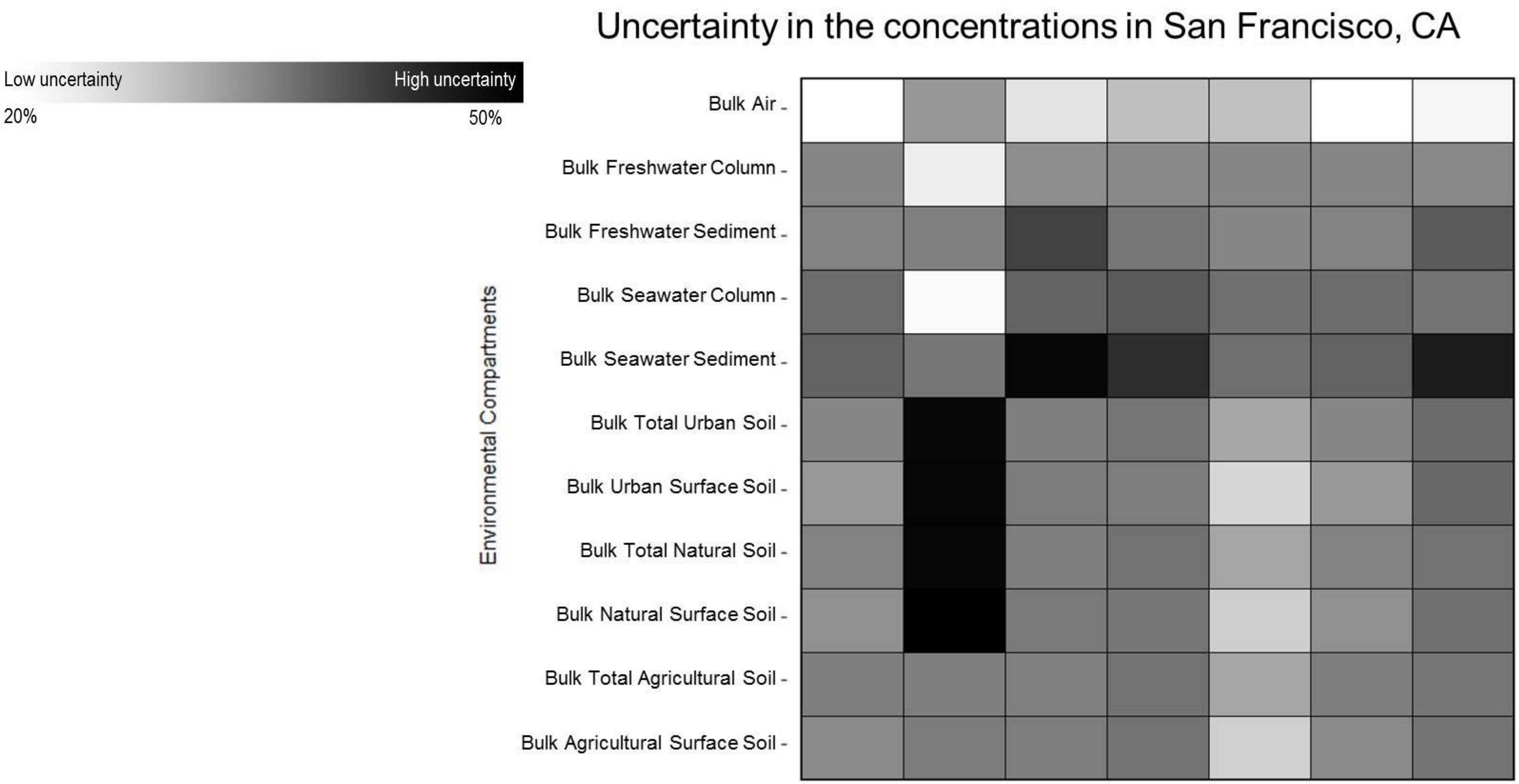
*labels removed for SW confidentiality

Fate & Transport Results

Daily concentration of Chemical "X" in New York City

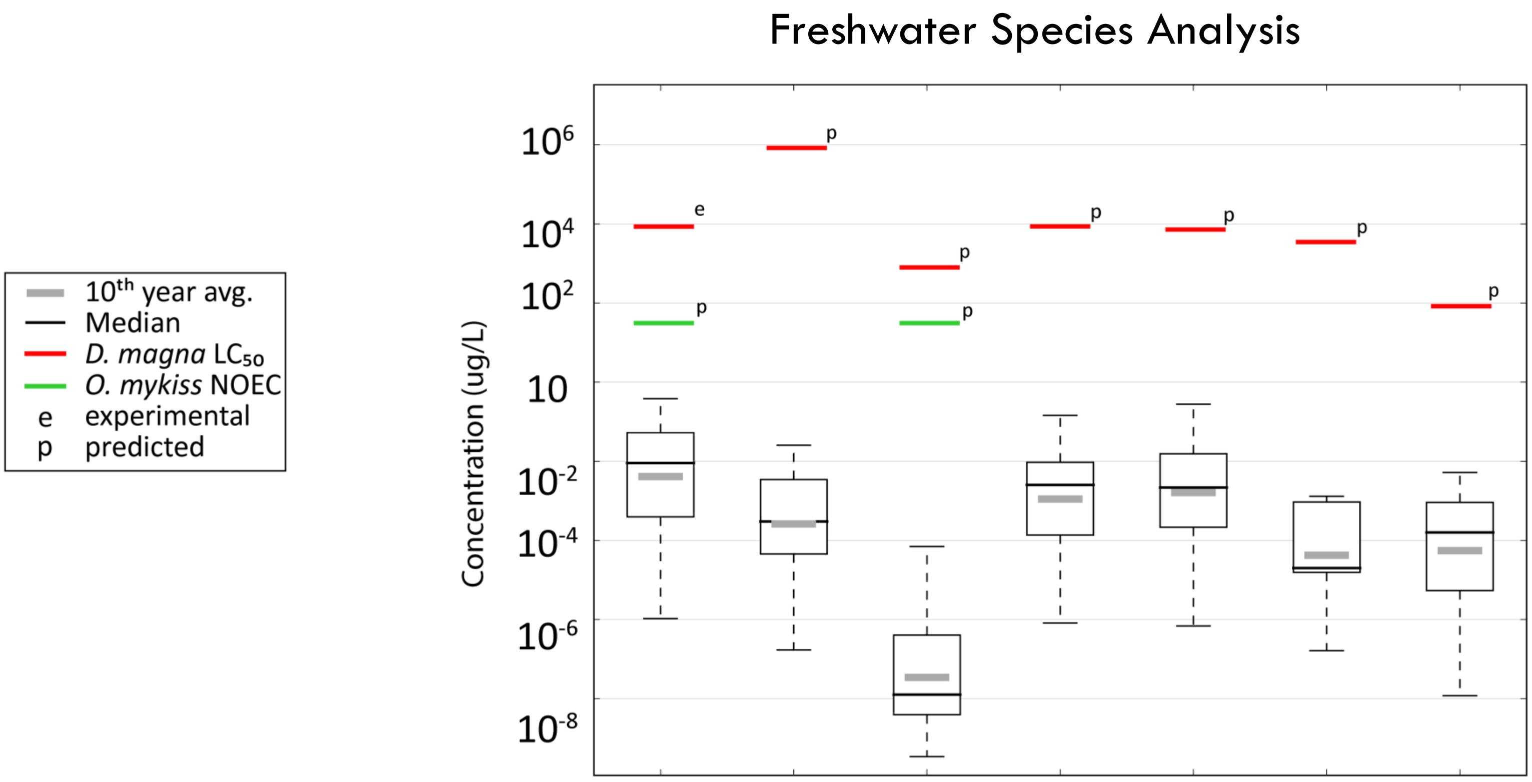


Fate & Transport Uncertainty Results



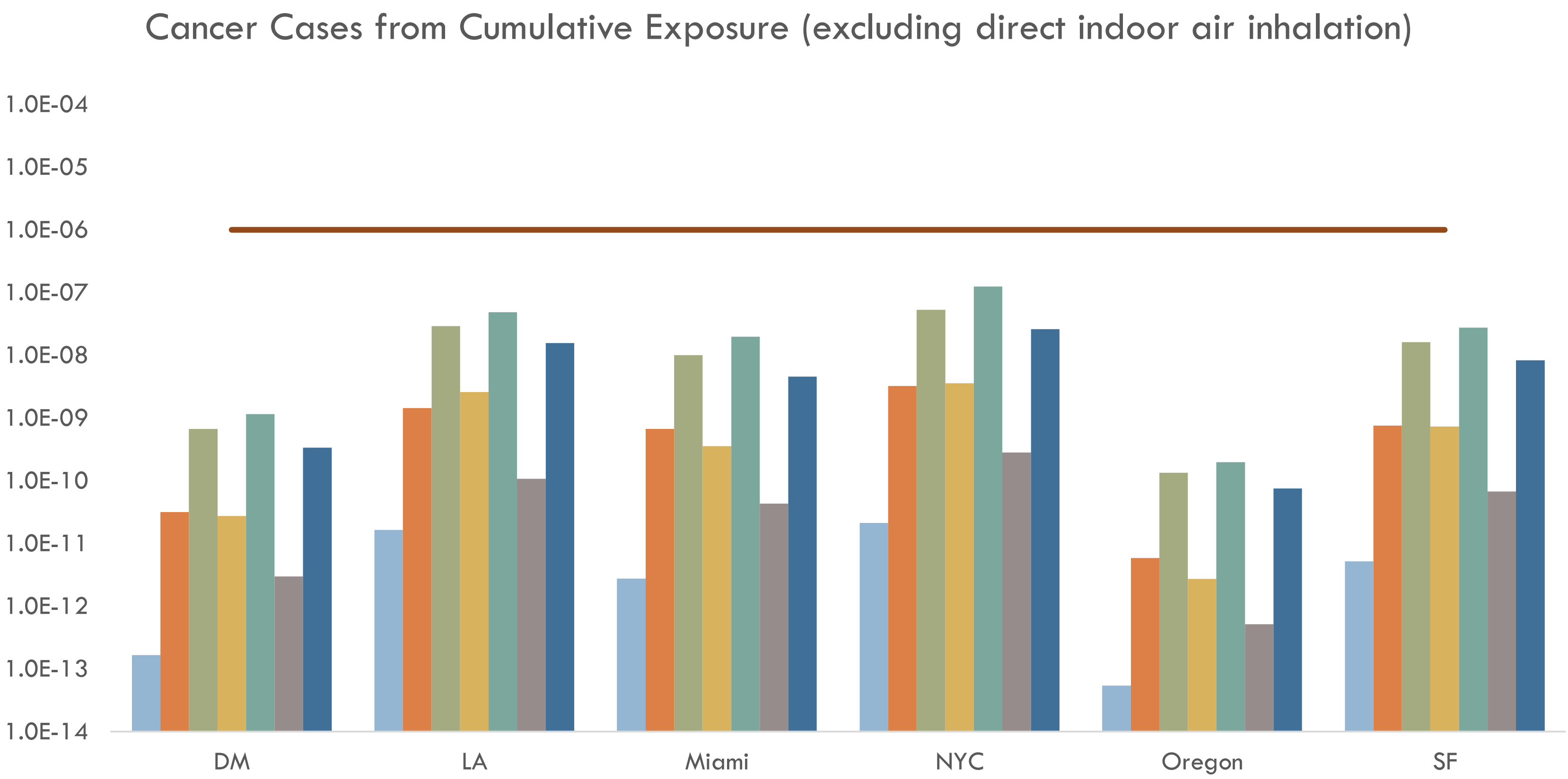
*labels removed for SW confidentiality

Ecotoxicity Results



*labels removed for SW confidentiality

Human Health Impact Results



*chemical labels removed for SW confidentiality

Review of Results

(1) Detailed report provided

(2) Conference call (at least 1hr) to go over the detailed results and summarize:

- Largest upstream impacts
- Use & Release quantities/ratios
- Downstream impacts

Clarifying questions answered in this presentation, but substantial questions are addressed in a follow up call after time for key stakeholders to review the results.

What we've learned so far…

Case studies have guided our model improvements and tool design, for example:

- Prioritization method for QSAR model results
- Necessity of supplemental reports describing data sources & methods in more detail
- Need for a more robust indoor air exposure model
- Providing relevant context for results is critical in effective communication

Other case study options

- Analyze specific chemical components within a product where data gaps exist
- Compare current/traditional chemical formulations to a proposed new formulation with novel chemical(s)
- Run a chemical (or group of chemicals) with existing LCIA results through the CLiCC models

We want your help!

- Want to participate in a case study?
- Have an idea for a way to test the CLiCC tool?

- Please contact Jess (PhD student researchers at the Bren School): JessicaLeePerkins@gmail.com

Final remarks

- Thank you for your attention and participation in this webinar
- This concludes the 2016 CLiCC Webinar series
- Any questions can be directed to presenters of this webinar or clicc@list.bren.ucsb.edu
- Recordings of the webinar available at clicc.ucsb.edu